

02/18/2009

10-576,971.trn

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NEWS 2 NOV 21 CAS patent coverage to include exemplified prophetic
substances identified in English-, French-, German-,
and Japanese-language basic patents from 2004-present
NEWS 3 NOV 26 MARPAT enhanced with FSORT command
NEWS 4 NOV 26 CHEMSAFE now available on STN Easy
NEWS 5 NOV 26 Two new SET commands increase convenience of STN
searching
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NEWS 7 DEC 12 GBFULL now offers single source for full-text
coverage of complete UK patent families
NEWS 8 DEC 17 Fifty-one pharmaceutical ingredients added to PS
NEWS 9 JAN 06 The retention policy for unread STNmail messages
will change in 2009 for STN-Columbus and STN-Tokyo
NEWS 10 JAN 07 WPIDS, WPINDEX, and WPIX enhanced Japanese Patent
Classification Data
NEWS 11 FEB 02 Simultaneous left and right truncation (SLART) added
for CERAB, COMPUAB, ELCOM, and SOLIDSTATE
NEWS 12 FEB 02 GENBANK enhanced with SET PLURALS and SET SPELLING
NEWS 13 FEB 06 Patent sequence location (PSL) data added to USGENE
NEWS 14 FEB 10 COMPENDEX reloaded and enhanced
NEWS 15 FEB 11 WTEXTILES reloaded and enhanced

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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* * * * * STN Columbus * * * * *

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FILE 'HOME' ENTERED AT 12:04:13 ON 17 FEB 2009

=> FIL CASREACT

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.22

0.22

FILE 'CASREACT' ENTERED AT 12:04:26 ON 17 FEB 2009

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FILE CONTENT:1840 - 8 Feb 2009 VOL 150 ISS 7

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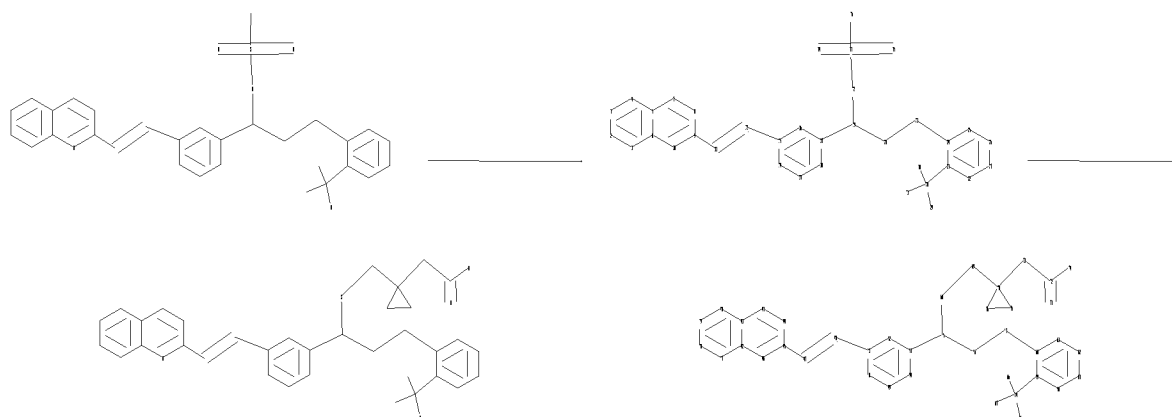
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*****
*
*      CASREACT now has more than 16.5 million reactions      *
*
*****
```

CASREACT contains reactions from CAS and from: ZIC/VINITI database (1974-1999) provided by InfoChem; INPI data prior to 1986; Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich; organic reactions, portions copyright 1996-2006 John Wiley & Sons, Ltd., John Wiley and Sons, Inc., Organic Reactions Inc., and Organic Syntheses Inc. Reproduced under license. All Rights Reserved.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

Uploading C:\Program Files\Stnexp\Queries\10-576,971.str



chain nodes :

11 12 19 20 21 28 29 30 31 32 33 34 35 36 47 48 55 56 57 64 65
66 67 68 69 71 72 73 74

ring nodes :

1 2 3 4 5 6 7 8 9 10 13 14 15 16 17 18 22 23 24 25 26 27 37
38 39 40 41 42 43 44 45 46 49 50 51 52 53 54 58 59 60 61 62 63
70 75 76

chain bonds :

9-11 11-12 12-15 17-19 19-20 19-32 20-21 21-24 23-28 28-29 28-30 28-31
32-33 33-34 33-35 33-36 45-47 47-48 48-51 53-55 55-56 55-68 56-57 57-60
59-64 64-65 64-66 64-67 68-69 69-70 70-71 71-72 72-73 72-74

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 13-14 13-18 14-15 15-16
16-17 17-18 22-23 22-27 23-24 24-25 25-26 26-27 37-38 37-42 38-39 39-40
40-41 41-42 41-43 42-46 43-44 44-45 45-46 49-50 49-54 50-51 51-52 52-53
53-54 58-59 58-63 59-60 60-61 61-62 62-63 70-75 70-76 75-76

exact/norm bonds :

19-32 28-29 32-33 33-34 33-35 33-36 55-68 64-65 68-69 72-73 72-74

exact bonds :

9-11 11-12 12-15 17-19 19-20 20-21 21-24 23-28 28-30 28-31 45-47 47-48
48-51 53-55 55-56 56-57 57-60 59-64 64-66 64-67 69-70 70-71 70-75 70-76
71-72 75-76

normalized bonds :

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1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 13-14 13-18 14-15 15-16
16-17 17-18 22-23 22-27 23-24 24-25 25-26 26-27 37-38 37-42 38-39 39-40
40-41 41-42 41-43 42-46 43-44 44-45 45-46 49-50 49-54 50-51 51-52 52-53
53-54 58-59 58-63 59-60 60-61 61-62 62-63

isolated ring systems :

containing 1 : 13 : 22 : 37 : 49 : 58 : 70 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
20:CLASS 21:CLASS 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:CLASS
29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS 36:CLASS
37:Atom 38:Atom 39:Atom 40:Atom 41:Atom 42:Atom 43:Atom 44:Atom 45:Atom
46:Atom 47:CLASS 48:CLASS 49:Atom 50:Atom 51:Atom 52:Atom 53:Atom 54:Atom
55:CLASS 56:CLASS 57:CLASS 58:Atom 59:Atom 60:Atom 61:Atom 62:Atom 63:Atom
64:CLASS 65:CLASS 66:CLASS 67:CLASS 68:CLASS 69:CLASS 70:Atom 71:CLASS
72:CLASS 73:CLASS 74:CLASS 75:Atom 76:Atom

fragments assigned reactant/reagent role:

containing 1

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss sam

SAMPLE SEARCH INITIATED 12:05:24 FILE 'CASREACT'

SCREENING COMPLETE - 2 REACTIONS TO VERIFY FROM 1 DOCUMENTS

100.0% DONE 2 VERIFIED 2 HIT RXNS 1 DOCS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED VERIFICATIONS: 2 TO 124

PROJECTED ANSWERS: 1 TO 79

L2 1 SEA SSS SAM L1 (2 REACTIONS)

=> s l1 sss full

FULL SEARCH INITIATED 12:05:52 FILE 'CASREACT'

SCREENING COMPLETE - 77 REACTIONS TO VERIFY FROM 21 DOCUMENTS

100.0% DONE 77 VERIFIED 57 HIT RXNS 16 DOCS

SEARCH TIME: 00.00.01

L3 16 SEA SSS FUL L1 (57 REACTIONS)

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=> d occ 1-

YOU HAVE REQUESTED DATA FROM 16 ANSWERS - CONTINUE? Y/(N):y

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L3 ANSWER 1 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS 2
NUMBER OF REACTIONS IN PATH 2
NUMBER OF REACTIONS IN SPATH 2
FIELD COUNT
RX(2) 2
RX(3) 2

L3 ANSWER 2 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS 6
NUMBER OF REACTIONS IN PATH 2
NUMBER OF REACTIONS IN SPATH 2
FIELD COUNT
RX(3) 2
RX(4) 2
RX(5) 2
RX(6) 2
RX(9) 2
RX(10) 2

L3 ANSWER 3 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS 1
NUMBER OF REACTIONS IN PATH 1
NUMBER OF REACTIONS IN SPATH 1
FIELD COUNT
RX(1) 2

L3 ANSWER 4 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS 1
NUMBER OF REACTIONS IN PATH 1
NUMBER OF REACTIONS IN SPATH 1
FIELD COUNT
RX(1) 2

02/18/2009

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L3	ANSWER 5 OF 16	CASREACT	COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS	5		
NUMBER OF REACTIONS IN PATH	3		
NUMBER OF REACTIONS IN SPATH	5		
FIELD	COUNT		
RX(1)	2		
RX(3)	2		
RX(6)	2		
RX(9)	2		
RX(12)	2		

L3	ANSWER 6 OF 16	CASREACT	COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS	4		
NUMBER OF REACTIONS IN PATH	1		
NUMBER OF REACTIONS IN SPATH	1		
FIELD	COUNT		
RX(4)	2		
RX(7)	2		
RX(9)	2		
RX(10)	2		

L3	ANSWER 7 OF 16	CASREACT	COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS	3		
NUMBER OF REACTIONS IN PATH	2		
NUMBER OF REACTIONS IN SPATH	3		
FIELD	COUNT		
RX(1)	2		
RX(3)	2		
RX(4)	2		

L3	ANSWER 8 OF 16	CASREACT	COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS	2		
NUMBER OF REACTIONS IN PATH	1		
NUMBER OF REACTIONS IN SPATH	2		
FIELD	COUNT		
RX(1)	2		
RX(3)	2		

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L3 ANSWER 9 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS 4
NUMBER OF REACTIONS IN PATH 1
NUMBER OF REACTIONS IN SPATH 2
FIELD COUNT
RX(1) 2
RX(6) 2
RX(10) 2
RX(13) 2

L3 ANSWER 10 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS 4
NUMBER OF REACTIONS IN PATH 4
NUMBER OF REACTIONS IN SPATH 4
FIELD COUNT
RX(1) 2
RX(2) 2
RX(3) 2
RX(4) 2

L3 ANSWER 11 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS 2
NUMBER OF REACTIONS IN PATH 2
NUMBER OF REACTIONS IN SPATH 2
FIELD COUNT
RX(2) 2
RX(3) 2

L3 ANSWER 12 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS 6
NUMBER OF REACTIONS IN PATH 2
NUMBER OF REACTIONS IN SPATH 2
FIELD COUNT
RX(13) 2
RX(15) 2
RX(22) 2
RX(24) 2
RX(25) 2
RX(30) 2

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L3 ANSWER 13 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS 2
NUMBER OF REACTIONS IN PATH 1
NUMBER OF REACTIONS IN SPATH 2
FIELD COUNT
RX(2) 2
RX(5) 2

L3 ANSWER 14 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS 2
NUMBER OF REACTIONS IN PATH 1
NUMBER OF REACTIONS IN SPATH 2
FIELD COUNT
RX(2) 2
RX(13) 2

L3 ANSWER 15 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS 1
NUMBER OF REACTIONS IN PATH 1
NUMBER OF REACTIONS IN SPATH 1
FIELD COUNT
RX(8) 2

L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS 12
NUMBER OF REACTIONS IN PATH 1
NUMBER OF REACTIONS IN SPATH 1
FIELD COUNT
RX(4) 2
RX(10) 2
RX(17) 2
RX(18) 2
RX(20) 2
RX(21) 2
RX(23) 2
RX(24) 2
RX(25) 2
RX(26) 2
RX(27) 2
RX(28) 2

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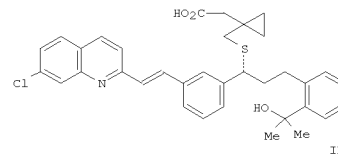
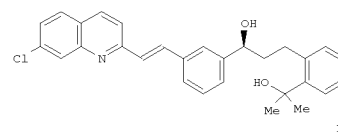
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L3 ANSWER 1 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 149:556456 CASREACT
 TITLE: Process for the purification of optically impure

2-(2-(3(S)-(3-(7-chloro-2-quinolinyl)ethenyl)phenyl)-3-hydroxy-propyl)phenyl-2-propanol
 INVENTOR(S): Salman, Ada; Gafni, Yael; Weisman, Alex; Perelmutter, Dihana; Levin, Inna; Noiman, Michal; Antler, Ofir
 PATENT ASSIGNEE(S): Chemagis Ltd., Israel
 SOURCE: PCT Int. Appl., 14pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

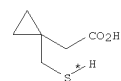
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008135966	A1	20081113	WO 2008-IL482	20080409
<p>W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW</p> <p>RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, BV, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM</p>				
PRIORITY APPLN. INFO.:		US 2007-915523P		20070502
GI				

L3 ANSWER 1 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



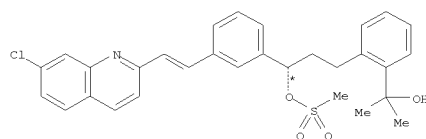
AB A process for purifying an optically impure 2-(2-(3(S)-(3-(7-chloro-2-quinolinyl)ethenyl)-phenyl)-3-(hydroxylpropyl)phenyl)-2-propanol (I) is disclosed. The purified compound typically has an enantiomeric excess higher than 99%, and can be used to prepare montelukast (II) and salts thereof.
 REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

RX(2) OF 5 ...G + C + H ==> I

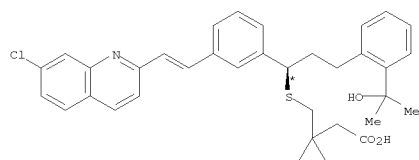
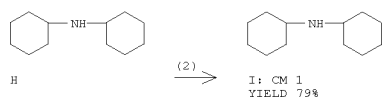


G

L3 ANSWER 1 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



C



I: CM 2
YIELD 79%

RX(2) RCT G 162515-68-6

STAGE(1)
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 10 minutes, room temperature
 SUBSTAGE(2) room temperature → -15 deg C

STAGE(2)
 RGT J 109-72-8 BuLi
 SOL 110-54-3 Hexane
 CON SUBSTAGE(1) 75 minutes, -5 deg C
 SUBSTAGE(2) 30 minutes, -5 deg C

STAGE(3)
 RCT C 807638-71-7

L3 ANSWER 1 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

SOL 109-99-9 THF
 CON SUBSTAGE(1) -5 deg C
 SUBSTAGE(2) -5 deg C

STAGE(4)
 RGT K 7647-14-5 NaCl
 SOL 141-78-6 AcOEt, 7732-18-5 Water
 CON SUBSTAGE(1) 75 minutes, -5 deg C
 SUBSTAGE(2) 8.5 hours, -5 deg C → room temperature

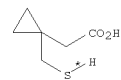
STAGE(5)
 SOL 141-78-6 AcOEt
 CON 30 minutes, 20 deg C

STAGE(6)
 RCT H 101-83-7
 CON 1 hour, 20 deg C

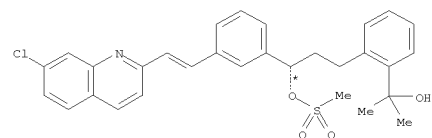
STAGE(7)
 SOL 110-54-3 Hexane
 CON SUBSTAGE(1) 2 hours, 20 deg C
 SUBSTAGE(2) overnight, 20 deg C

PRO I 577953-88-9
 NTE fourth stage quench; sixth stage seeding after clear soln.

RX(3) OF 5 ...G + C ==> P



G



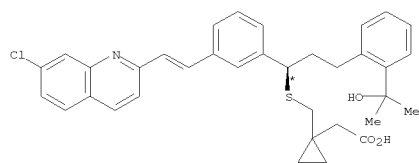
C

(3) →

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L3 ANSWER 1 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



P

RX(3) RCT G 162515-68-6

STAGE(1)
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 10 minutes, room temperature
 SUBSTAGE(2) room temperature -> -15 deg C

STAGE(2)
 RGT J 109-72-8 BuLi
 SOL 110-54-3 Hexane
 CON SUBSTAGE(1) 75 minutes, -5 deg C
 SUBSTAGE(2) 30 minutes, -5 deg C

STAGE(3)
 RCT C 807638-71-7
 SOL 109-99-9 THF
 CON SUBSTAGE(1) -5 deg C
 SUBSTAGE(2) -5 deg C

STAGE(4)
 RGT K 7647-14-5 NaCl
 SOL 141-78-6 AcOEt, 7732-18-5 Water
 CON SUBSTAGE(1) 75 minutes, -5 deg C
 SUBSTAGE(2) 8.5 hours, -5 deg C -> room temperature

STAGE(5)
 SOL 141-78-6 AcOEt
 CON 30 minutes, 20 deg C

STAGE(6)
 RGT H 101-83-7 Dicyclohexylamine
 CON 1 hour, 20 deg C

L3 ANSWER 1 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

STAGE(7)
 SOL 110-54-3 Hexane
 CON SUBSTAGE(1) 2 hours, 20 deg C
 SUBSTAGE(2) overnight, 20 deg C

STAGE(8)
 SOL 108-88-3 PhMe, 7732-18-5 Water
 CON room temperature

STAGE(9)
 RGT Q 64-19-7 AcOH
 SOL 7732-18-5 Water
 CON 10 minutes, 20 - 25 deg C

STAGE(10)
 SOL 7732-18-5 Water
 CON 10 minutes, 20 - 25 deg C

STAGE(11)
 RGT R 1310-73-2 NaOH
 SOL 7732-18-5 Water, 64-17-5 EtOH
 CON SUBSTAGE(1) 10 minutes, 20 - 25 deg C
 SUBSTAGE(2) 10 minutes, 20 - 25 deg C

STAGE(12)
 SOL 75-05-8 MeCN
 CON SUBSTAGE(1) 20 minutes, 40 deg C
 SUBSTAGE(2) 1.5 hours, 40 deg C

STAGE(13)
 SOL 75-05-8 MeCN
 CON SUBSTAGE(1) 20 minutes, 40 deg C
 SUBSTAGE(2) 1 hour, 40 deg C

STAGE(14)
 SOL 75-05-8 MeCN
 CON SUBSTAGE(1) 20 minutes, 40 deg C
 SUBSTAGE(2) 1 hour, 40 deg C

PRO P 151767-02-1
 NTE fourth stage quench; sixth stage seeding after clear soln.

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YOU HAVE REQUESTED DATA FROM 16 ANSWERS - CONTINUE? Y/(N):y

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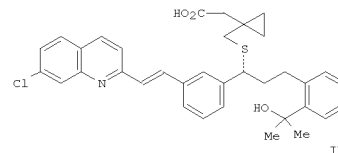
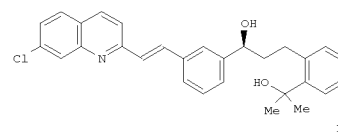
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L3 ANSWER 1 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 149:556456 CASREACT
 TITLE: Process for the purification of optically impure

2-(2-(3(S)-(3-(7-chloro-2-quinolinyl)ethenyl)phenyl)-3-hydroxy-propyl)phenyl-2-propanol
 INVENTOR(S): Salman, Ada; Gafni, Yael; Weisman, Alex; Perelmutter, Dihana; Levin, Inna; Noiman, Michal; Antler, Ofir
 PATENT ASSIGNEE(S): Chemagis Ltd., Israel
 SOURCE: PCT Int. Appl., 14pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

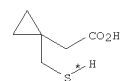
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008135966	A1	20081113	WO 2008-IL482	20080409
<p>W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW</p> <p>RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM</p>				
PRIORITY APPLN. INFO.:		US 2007-915523P 20070502		
GI				

L3 ANSWER 1 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



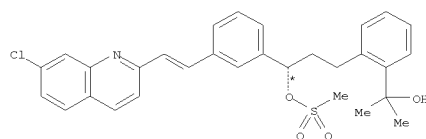
AB A process for purifying an optically impure 2-(2-(3(S)-(3-(7-chloro-2-quinolinyl)ethenyl)-phenyl)-3-(hydroxylpropyl)phenyl)-2-propanol (I) is disclosed. The purified compound typically has an enantiomeric excess higher than 99%, and can be used to prepare montelukast (II) and salts thereof.
 REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

RX(2) OF 5 ...G + C + H ==> I

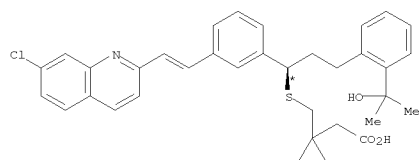
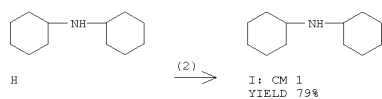


G

L3 ANSWER 1 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



C



I: CM 2
YIELD 79%

RX(2) RCT G 162515-68-6

STAGE(1)
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 10 minutes, room temperature
 SUBSTAGE(2) room temperature → -15 deg C

STAGE(2)
 RGT J 109-72-8 BuLi
 SOL 110-54-3 Hexane
 CON SUBSTAGE(1) 75 minutes, -5 deg C
 SUBSTAGE(2) 30 minutes, -5 deg C

STAGE(3)
 RCT C 807638-71-7

L3 ANSWER 1 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

SOL 109-99-9 THF
 CON SUBSTAGE(1) -5 deg C
 SUBSTAGE(2) -5 deg C

STAGE(4)
 RGT K 7647-14-5 NaCl
 SOL 141-78-6 AcOEt, 7732-18-5 Water
 CON SUBSTAGE(1) 75 minutes, -5 deg C
 SUBSTAGE(2) 8.5 hours, -5 deg C → room temperature

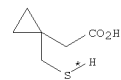
STAGE(5)
 SOL 141-78-6 AcOEt
 CON 30 minutes, 20 deg C

STAGE(6)
 RCT H 101-83-7
 CON 1 hour, 20 deg C

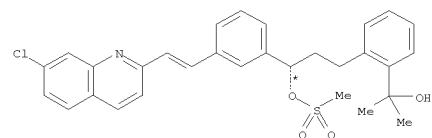
STAGE(7)
 SOL 110-54-3 Hexane
 CON SUBSTAGE(1) 2 hours, 20 deg C
 SUBSTAGE(2) overnight, 20 deg C

PRO I 577953-88-9
 NTE fourth stage quench; sixth stage seeding after clear soln.

RX(3) OF 5 ...G + C ==> P



G



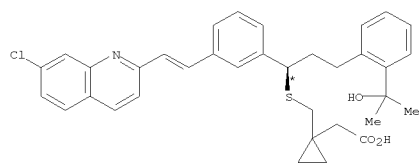
C

(3) →

02/18/2009

10-576,971.trn

L3 ANSWER 1 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



● Na

P

RX(3) RCT G 162515-68-6

STAGE(1)
SOL 109-99-9 THF
CON SUBSTAGE(1) 10 minutes, room temperature
SUBSTAGE(2) room temperature -> -15 deg C

STAGE(2)
RGT J 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 75 minutes, -5 deg C
SUBSTAGE(2) 30 minutes, -5 deg C

STAGE(3)
RCT C 807638-71-7
SOL 109-99-9 THF
CON SUBSTAGE(1) -5 deg C
SUBSTAGE(2) -5 deg C

STAGE(4)
RGT K 7647-14-5 NaCl
SOL 141-78-6 AcOEt, 7732-18-5 Water
CON SUBSTAGE(1) 75 minutes, -5 deg C
SUBSTAGE(2) 8.5 hours, -5 deg C -> room temperature

STAGE(5)
SOL 141-78-6 AcOEt
CON 30 minutes, 20 deg C

STAGE(6)
RGT H 101-83-7 Dicyclohexylamine
CON 1 hour, 20 deg C

L3 ANSWER 2 OF 16 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 149:556455 CASREACT
TITLE: Process for the preparation of amorphous Montelukast sodium salt wherein crystalline forms of methanesulfonate intermediate and Montelukast are not isolated.

INVENTOR(S): Zyla, Daniel; Rynkiewicz, Robert; Krzyzanowski, Mariusz; Ramza, Jan

PATENT ASSIGNEE(S): Zakłady Farmaceutyczne Polpharma S. A., Pol.

SOURCE: PCT Int. Appl., 22pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008136693	A2	20081113	WO 2008-PL33	20080430
WO 2008136693	A3	20081231		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, NZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: PL 2007-382346 20070502

AB Amorphous Montelukast sodium was prepared by (1) reaction of 2-[[2-(3S)-[3-[2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-(hydroxypropyl)phenyl]-2-propanol with MeSO₂Cl in the presence of a tertiary amine, (2) filtration of precipitated tertiary amine salt and reaction of the crude methanesulfonate ester with [1-(mercaptomethyl)cyclopropyl]acetic acid disodium salt, (3) isolation of crystalline 1-[[[1(R)-[3-[2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]sulfanyl]methyl]cyclopropaneacetic acid tert-butylamine salt, (4) purification of this salt until the product has high pharmaceutical purity, and (5) conversion of the purified salt to the title compound

RX(3) OF 10 ...G + B + I ==> J

L3 ANSWER 1 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

STAGE(7)
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 2 hours, 20 deg C
SUBSTAGE(2) overnight, 20 deg C

STAGE(8)
SOL 108-88-3 PhMe, 7732-18-5 Water
CON room temperature

STAGE(9)
RGT Q 64-19-7 AcOH
SOL 7732-18-5 Water
CON 10 minutes, 20 - 25 deg C

STAGE(10)
SOL 7732-18-5 Water
CON 10 minutes, 20 - 25 deg C

STAGE(11)
RGT R 1310-73-2 NaOH
SOL 7732-18-5 Water, 64-17-5 EtOH
CON SUBSTAGE(1) 10 minutes, 20 - 25 deg C
SUBSTAGE(2) 10 minutes, 20 - 25 deg C

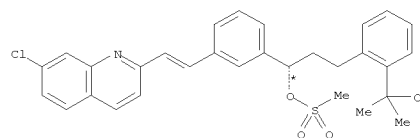
STAGE(12)
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 20 minutes, 40 deg C
SUBSTAGE(2) 1.5 hours, 40 deg C

STAGE(13)
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 20 minutes, 40 deg C
SUBSTAGE(2) 1 hour, 40 deg C

STAGE(14)
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 20 minutes, 40 deg C
SUBSTAGE(2) 1 hour, 40 deg C

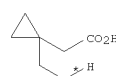
PRO P 151767-02-1
NTE fourth stage quench; sixth stage seeding after clear soln.

L3 ANSWER 2 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



● Na

G



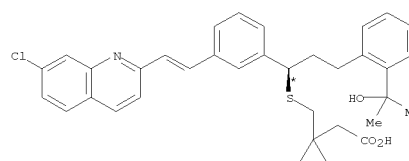
● 2 Na

B



(3)

J: CM 1



J: CM 2

RX(3) RCT G 1079902-34-3, B 884842-91-5

STAGE(1)
CON SUBSTAGE(2) 12 hours, 10 - 15 deg C

02/18/2009

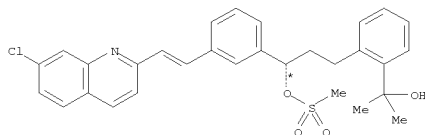
10-576,971.trn

L3 ANSWER 2 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

STAGE(2)
 RCT I 75-64-9
 CON SUBSTAGE(2) 30 minutes

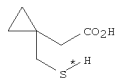
PRO J 851755-58-3
 NTE workup

RX(4) OF 10 ...G + B ==> K



● Na

G

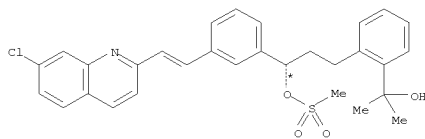


● 2 Na

B



L3 ANSWER 2 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

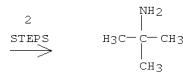


● Na

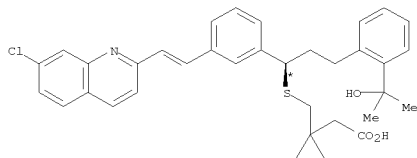
G



I



J: CM 1

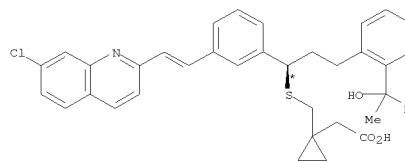


J: CM 2

RX(1) RCT A 162515-68-6
 RGT C 865-48-5 NaOBu-t
 PRO B 884842-91-5
 SOL 68-12-2 DMF
 CON SUBSTAGE(1) 20+/-5 deg C
 SUBSTAGE(3) 1 hour, >15 deg C

RX(3) RCT G 1079902-34-3, B 884842-91-5

L3 ANSWER 2 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



● Na

K

RX(4) RCT G 1079902-34-3, B 884842-91-5

STAGE(1)
 CON SUBSTAGE(2) 12 hours, 10 - 15 deg C

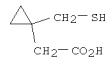
STAGE(2)
 RGT I 75-64-9 t-BuNH2
 CON SUBSTAGE(2) 30 minutes

STAGE(3)
 RGT L 64-19-7 AcOH
 SOL 7732-18-5 Water
 CON room temperature

STAGE(4)
 RGT M 1310-73-2 NaOH
 SOL 67-56-1 MeOH
 CON room temperature

PRO K 151767-02-1

RX(5) OF 10 COMPOSED OF RX(1), RX(3)
 RX(5) A + G + I ==> J



A

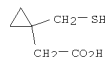
L3 ANSWER 2 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

STAGE(1)
 CON SUBSTAGE(2) 12 hours, 10 - 15 deg C

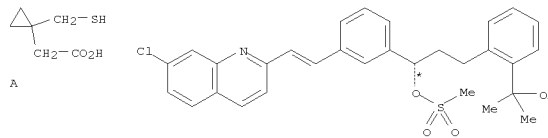
STAGE(2)
 RCT I 75-64-9
 CON SUBSTAGE(2) 30 minutes

PRO J 851755-58-3
 NTE workup

RX(6) OF 10 COMPOSED OF RX(1), RX(4)
 RX(6) A + G ==> K

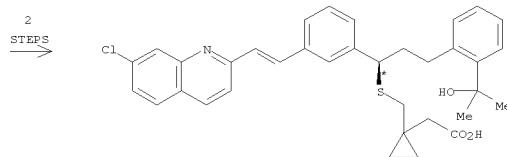


A



● Na

G



● Na

K

RX(1) RCT A 162515-68-6
 RGT C 865-48-5 NaOBu-t
 PRO B 884842-91-5

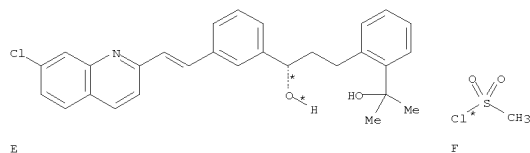
02/18/2009

10-576,971.trn

L3 ANSWER 2 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)
 SOL 68-12-2 DMF
 CON SUBSTAGE(1) 20+/-5 deg C
 SUBSTAGE(3) 1 hour, >15 deg C

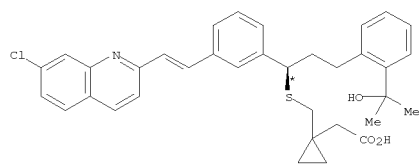
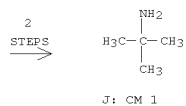
RX(4) RCT G 1079902-34-3, B 884842-91-5
 STAGE(1)
 CON SUBSTAGE(2) 12 hours, 10 - 15 deg C
 STAGE(2)
 RGT I 75-64-9 t-BuNH2
 CON SUBSTAGE(2) 30 minutes
 STAGE(3)
 RGT L 64-19-7 AcOH
 SOL 7732-18-5 Water
 CON room temperature
 STAGE(4)
 RGT M 1310-73-2 NaOH
 SOL 67-56-1 MeOH
 CON room temperature
 PRO K 151767-02-1

RX(9) OF 10 COMPOSED OF REACTION SEQUENCE RX(2), RX(3)
 AND REACTION SEQUENCE RX(1), RX(3)
 ...E + F ==> G...
 ...A + G + I ==> J



2
 STEPS
 →

L3 ANSWER 2 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



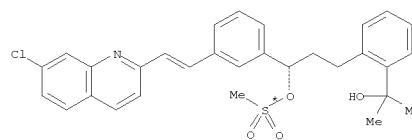
RX(2) RCT E 287930-77-2, F 124-63-0
 RGT H 121-44-8 Et3N
 PRO G 1079902-34-3
 SOL 68-12-2 DMF
 CON SUBSTAGE(1) room temperature -> -15 deg C
 SUBSTAGE(2) -20 - -15 deg C
 SUBSTAGE(3) 40 minutes

RX(1) RCT A 162515-68-6
 RGT C 865-48-5 NaOBu-t
 PRO B 884842-91-5
 SOL 68-12-2 DMF
 CON SUBSTAGE(1) 20+/-5 deg C
 SUBSTAGE(3) 1 hour, >15 deg C

RX(3) RCT G 1079902-34-3, B 884842-91-5
 STAGE(1)
 CON SUBSTAGE(2) 12 hours, 10 - 15 deg C
 STAGE(2)
 RCT I 75-64-9
 CON SUBSTAGE(2) 30 minutes
 PRO J 851755-58-3
 NTE workup

RX(10) OF 10 COMPOSED OF REACTION SEQUENCE RX(2), RX(4)
 AND REACTION SEQUENCE RX(1), RX(4)

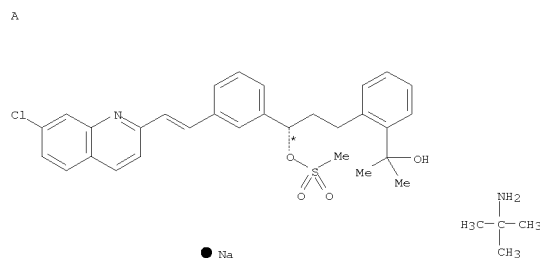
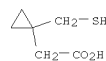
L3 ANSWER 2 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



● Na

G

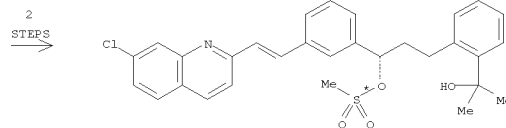
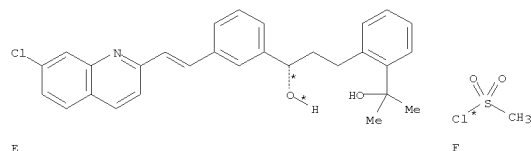
START NEXT REACTION SEQUENCE



G

L3 ANSWER 2 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

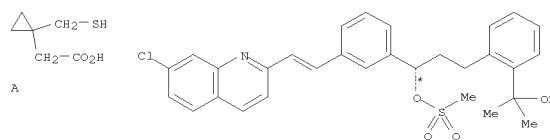
...E + F ==> G...
 ...A + G ==> K



● Na

G

START NEXT REACTION SEQUENCE



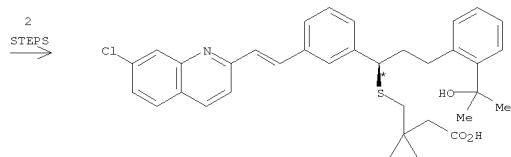
● Na

G

02/18/2009

10-576,971.trn

L3 ANSWER 2 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



● Na

K

RX(2) RCT E 287930-77-2, F 124-63-0
RGT H 121-44-8 Et3N
PRO G 1079902-34-3
SOL 68-12-2 DMF
CON SUBSTAGE(1) room temperature -> -15 deg C
SUBSTAGE(2) -20 - -15 deg C
SUBSTAGE(3) 40 minutes

RX(1) RCT A 162515-68-6
RGT C 865-48-5 NaOBu-t
PRO B 884842-91-5
SOL 68-12-2 DMF
CON SUBSTAGE(1) 20+/-5 deg C
SUBSTAGE(3) 1 hour, >15 deg C

RX(4) RCT G 1079902-34-3, B 884842-91-5

STAGE(1)
CON SUBSTAGE(2) 12 hours, 10 - 15 deg C

STAGE(2)
RGT I 75-64-9 t-BuNH2
CON SUBSTAGE(2) 30 minutes

STAGE(3)
RGT L 64-19-7 AcOH
SOL 7732-18-5 Water
CON room temperature

STAGE(4)
RGT M 1310-73-2 NaOH
SOL 67-56-1 MeOH

L3 ANSWER 3 OF 16 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 149:176195 CASREACT
TITLE: Process for preparation of montelukast
INVENTOR(S): Halama, Ales; Jirman, Josef
PATENT ASSIGNEE(S): Zentiva, A.S., Czech Rep.
SOURCE: PCT Int. Appl., 2ipp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008083635	A1	20080717	WO 2008-CZ2	20080108
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: CZ 2007-20 20070109
OTHER SOURCE(S): MARPAT 149:176195
AB The present invention pertains to a process for the preparation of montelukast, characterized in that a polyether, i.e. polyethyleneglycol or a crown-ether, was used as a phase transfer catalyst, which can solvate metal ions, hence, increase the solubility and reactivity of nucleophilic reagents. The increased reactivity of nucleophilic reagents resulted in higher selectivity of the process, i.e. the impact of unwanted competitive reactions that led to formation of impurities was suppressed. For example, [1-(mercaptomethyl)cyclopropyl]acetic acid, potassium tert-amylate, and 18-crown-6 were stirred in toluene under argon at -10 °C to give a slurry. A solution of 2-[2-[(3S)-3-[3-[(2E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[(methanesulfonyl)oxy]propyl]phenyl]-2-propanol in THF was added to the slurry obtained above, which was stirred gradually from -10 °C to 21 °C for 1 h, and then stirred at 21 °C for several hours to afford montelukast in 92.7% conversion rate by HPLC.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

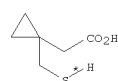
FORMAT

RX(1) OF 1 A + B ==> C

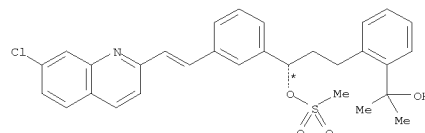
L3 ANSWER 2 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)
CON room temperature

PRO K 151767-02-1

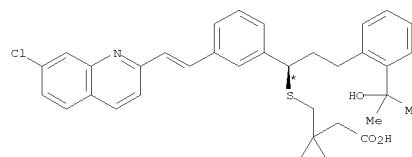
L3 ANSWER 3 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



A



B



C

RX(1) RCT A 162515-68-6, B 807638-71-7
RGT D 1907-33-1 Li tert-butoxide
PRO C 158966-92-8
SOL 109-99-9 THF, 108-88-3 PhMe
CON SUBSTAGE(1) 21 deg C -> -10 deg C
SUBSTAGE(2) -10 deg C
SUBSTAGE(3) 1 hour, -10 deg C -> 21 deg C
SUBSTAGE(4) >1 hour, 21 deg C
NTE optimization study

02/18/2009

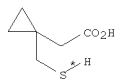
10-576,971.trn

L3 ANSWER 4 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 148:538087 CASREACT
 TITLE: Improved process for preparation of
 (R)-(E)-1-[[1-[3-[2-[7-chloro-2-quinolinyl]ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]thio]methyl]cyclopropaneacetic acid
 acid
 dicyclohexylamine salt (montelukast dicyclohexylamine salt)
 INVENTOR(S): Reguri, Buchi Reddy; Bollikonda, Satyanarayana; Bulusu, Veera Venkata Naga Chandra Sekhar
 PATENT ASSIGNEE(S): Dr. Reddy's Laboratories Limited, India
 SOURCE: Indian Pat. Appl., 10pp.
 CODEN: INXXBQ
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 2002MA00307	A	20070803	IN 2002-MA307	20020422
PRIORITY APPLN. INFO.: IN 2002-MA307 20020422				

AB The present invention provides the novel recrystn. method for the preparation of (R)-(E)-1-[[1-[3-[2-[7-chloro-2-quinolinyl]ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]thio]methyl]cyclopropaneacetic acid dicyclohexylamine salt (montelukast dicyclohexylamine salt). The novel recrystn. method involves the purification of crude montelukast dicyclohexylamine salt in a mixture of nitriles and alcs. such as acetonitrile and methanol or 2-propanol.

RX(1) OF 1 A + B + C ==> D

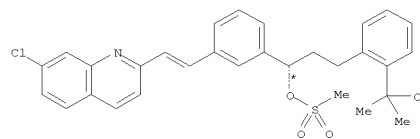


A

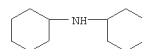
L3 ANSWER 4 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)
 SUBSTAGE(2) 10 - 12 hours, -5 - 0 deg C

STAGE(3)
 RCT C 101-83-7
 SOL 141-78-6 AcOEt
 PRO D 577953-88-9

L3 ANSWER 4 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

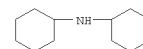


B

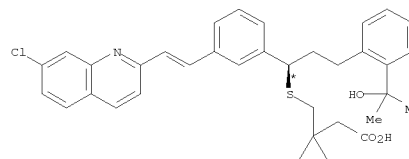


C

(1) →



D: CM 1



D: CM 2

RX(1) RCT A 162515-68-6

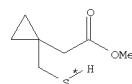
STAGE(1)
 RCT E 109-72-8 BuLi
 SOL 109-99-9 THF
 CON SUBSTAGE(1) room temperature -> -15 deg C
 SUBSTAGE(2) 1 hour, <-10 deg C
 SUBSTAGE(3) 30 minutes, <-10 deg C
 STAGE(2)
 RCT B 807638-71-7
 SOL 109-99-9 THF
 CON SUBSTAGE(1) -10 deg C

L3 ANSWER 5 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 148:121604 CASREACT
 TITLE: A process for the preparation of leukotriene receptor antagonist (montelukast sodium)
 INVENTOR(S): Ray, Uttam Kumar; Boju, Sreenivasulu; Pathuri, Sreenivasa Rao; Meenakshisunderam, Sivakumaran
 PATENT ASSIGNEE(S): Aurobindo Pharma Limited, India
 SOURCE: PCT Int. Appl., 23pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008001213	A1	20080103	WO 2007-1B1870	20070625

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 IN 2006CH01084 A 20081128 IN 2006-CH1084 20060626
 IN 2006CH01085 A 20081128 IN 2006-CH1085 20060626
 PRIORITY APPLN. INFO.: IN 2006-CH1084 20060626
 IN 2006-CH1085 20060626
 AB The invention relates to a process for the preparation of 1-[[[(1R)-1-[3-[(1E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]-cyclopropaneacetic acid, monosodium salt, known as montelukast sodium.
 REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

RX(1) OF 14 ...A + B ==> C

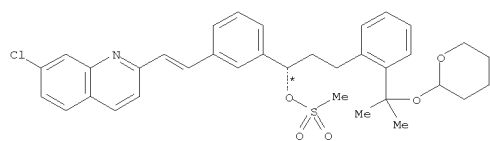


A

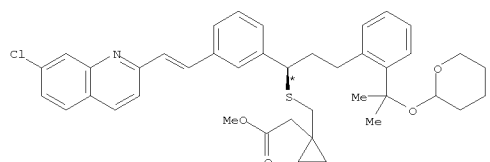
02/18/2009

10-576,971.trn

L3 ANSWER 5 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



B



C

YIELD 73%

RX(1) RCT A 152922-73-1, B 162489-71-6
 RGT D 584-08-7 K₂CO₃
 PRO C 1000788-70-4
 SOL 75-05-8 MeCN
 CON SUBSTAGE(1) 27 - 30 deg C
 SUBSTAGE(2) 1 hour, -5 - 0 deg C
 SUBSTAGE(3) 0 deg C -> 30 deg C
 SUBSTAGE(4) 36 hours, 27 - 30 deg C

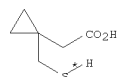
RX(3) OF 14 ...H + A ==> K...

L3 ANSWER 5 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

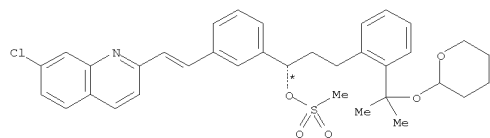
CON SUBSTAGE(1) 15 minutes, -5 - 0 deg C
 SUBSTAGE(2) 0 deg C -> 20 deg C
 SUBSTAGE(3) 16 hours, 20 - 25 deg C

PRO K 855473-51-7

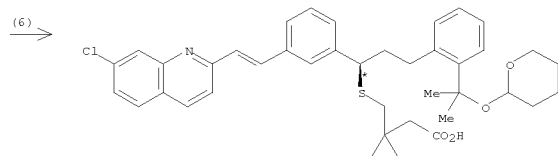
RX(6) OF 14 ...T + B ==> U...



T



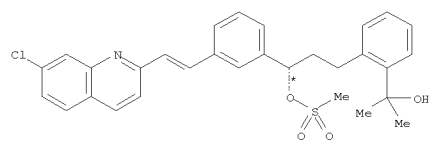
B



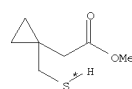
U

RX(6) RCT T 162515-68-6
 STAGE(1)
 RGT V 109-72-8 BuLi
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 25 - 30 deg C
 SUBSTAGE(2) 30 deg C -> -15 deg C
 SUBSTAGE(3) 30 minutes, -5 deg C

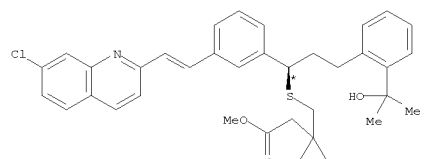
L3 ANSWER 5 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



H



A



K

YIELD 99%

RX(3) RCT H 807638-71-7

STAGE(1)
 RGT D 584-08-7 K₂CO₃
 SOL 75-05-8 MeCN
 CON -5 deg C

STAGE(2)
 RCT A 152922-73-1
 SOL 75-05-8 MeCN

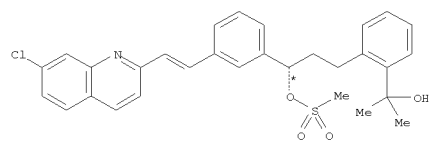
L3 ANSWER 5 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

STAGE(2)
 RCT B 162489-71-6
 SOL 109-99-9 THF
 CON SUBSTAGE(1) -10 - -5 deg C
 SUBSTAGE(2) 8 hours, -5 deg C

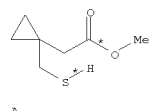
PRO U 1000788-71-5

RX(9) OF 14 COMPOSED OF RX(3), RX(4)

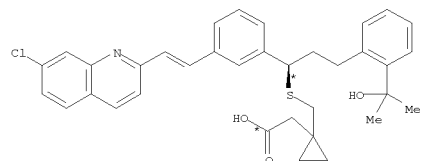
RX(9) H + A ==> L



H



A



L

RX(3) RCT H 807638-71-7

02/18/2009

10-576,971.trn

L3 ANSWER 5 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

STAGE(1)
 RGT D 584-08-7 K2CO3
 SOL 75-05-8 MeCN
 CON -5 deg C

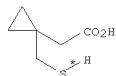
STAGE(2)
 RCT A 152922-73-1
 SOL 75-05-8 MeCN
 SUBSTAGE(1) 15 minutes, -5 - 0 deg C
 SUBSTAGE(2) 0 deg C -> 20 deg C
 SUBSTAGE(3) 16 hours, 20 - 25 deg C

PRO K 855473-51-7

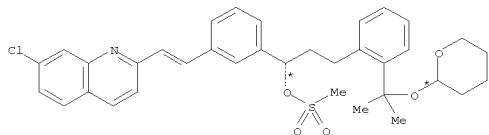
RX(4) RCT K 855473-51-7
 RGT M 1310-73-2 NaOH
 PRO L 158966-92-8
 SOL 109-99-9 THF, 67-56-1 MeOH, 7732-18-5 Water
 CON SUBSTAGE(1) room temperature -> 0 deg C
 SUBSTAGE(2) 2 days, room temperature

RX(12) OF 14 COMPOSED OF RX(6), RX(7)

RX(12) T + B ==> L



T



B

L3 ANSWER 6 OF 16 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 147:257460 CASREACT
 TITLE: Process for preparation of
 1-(mercaptomethyl)cyclopropaneacetic acid
 INVENTOR(S): Wang, Yanling; Wang, Yuang; Brand, Michael; Kaspi,
 Joseph
 PATENT ASSIGNEE(S): Chemagis Ltd., Israel
 SOURCE: PCT Int. Appl., 19pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007088545	A2	20070809	WO 2007-IL133	20070201
WO 2007088545	A3	20080124		

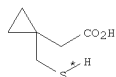
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

US 20070208177 A1 20070906 US 2007-700867 20070201
 PRIORITY APPLN. INFO.: US 2006-764347P 20060202

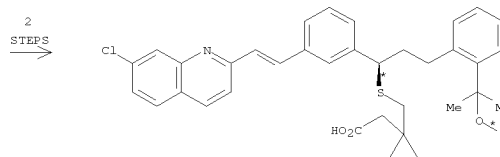
AB The present invention pertains to a process for the preparation of 1-(mercaptomethyl)cyclopropaneacetic acid as an intermediate for montelukast. For example, com. available 1-(hydroxymethyl)cyclopropaneacetonitrile was treated bromine/triphenyl phosphine for 1-(bromomethyl)cyclopropaneacetonitrile, which was then reacted with thiourea to give an intermediate. The intermediate obtained above was treated with sodium hydroxide solution to give 1-(mercaptomethyl)cyclopropaneacetic acid as novel montelukast intermediate. According to the present invention, by using this intermediate, montelukast acid and salts thereof are obtained in a simple and straightforward process.

RX(4) OF 10 ...I + N + O ==> P



I

L3 ANSWER 5 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



L

RX(6) RCT T 162515-68-6

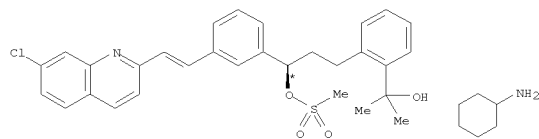
STAGE(1)
 RGT V 109-72-8 BuLi
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 25 - 30 deg C
 SUBSTAGE(2) 30 deg C -> -15 deg C
 SUBSTAGE(3) 30 minutes, -5 deg C

STAGE(2)
 RCT B 162489-71-6
 SOL 109-99-9 THF
 CON SUBSTAGE(1) -10 - -5 deg C
 SUBSTAGE(2) 8 hours, -5 deg C

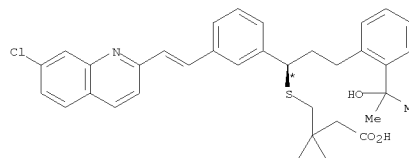
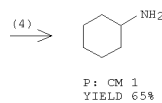
PRO U 1000788-71-5

RX(7) RCT U 1000788-71-5
 RGT W 24057-28-1 Pyridinium tosylate
 PRO L 158966-92-8
 SOL 109-99-9 THF, 67-56-1 MeOH
 CON SUBSTAGE(1) room temperature -> 60 deg C
 SUBSTAGE(2) 12 hours, 60 deg C

L3 ANSWER 6 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



N



P: CM 2
 YIELD 65%

RX(4) RCT I 162515-68-6

STAGE(1)
 RGT J 1310-73-2 NaOH
 SOL 68-12-2 DMF, 7732-18-5 Water
 CON 10 minutes, room temperature

STAGE(2)
 RCT N 920739-17-9
 SOL 109-99-9 THF
 CON 2 hours, 25 deg C

STAGE(3)
 RCT O 108-91-8

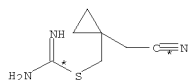
02/18/2009

10-576,971.trn

L3 ANSWER 6 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)
 SOL 141-78-6 AcOEt
 CON 25 deg C

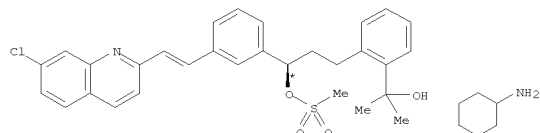
PRO P 945934-73-6

RX(7) OF 10 COMPOSED OF RX(3), RX(4)
 RX(7) G + N + O ==> P

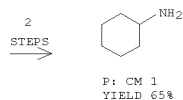


● HBr

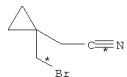
G



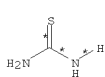
N



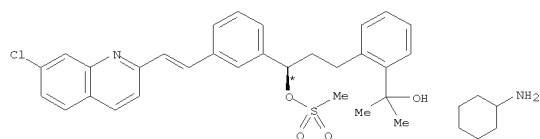
L3 ANSWER 6 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)
 RX(9) B + F + N + O ==> P



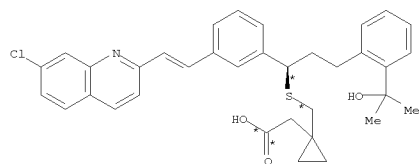
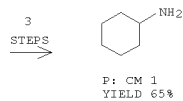
B



F



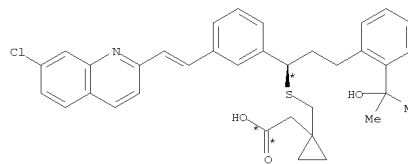
N



P: CM 2
YIELD 65%

RX(2) RCT B 338392-48-6, F 62-56-6
 PRO G 945934-74-7

L3 ANSWER 6 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



P: CM 2
YIELD 65%

RX(3) RCT G 945934-74-7

STAGE(1)

RGT J 1310-73-2 NaOH
 SOL 7732-18-5 Water
 CON SUBSTAGE(1) 14 hours, room temperature -> reflux
 SUBSTAGE(2) reflux -> room temperature

STAGE(2)

RGT K 64-18-6 HCO2H
 SOL 141-78-6 AcOEt
 CON -5 - 5 deg C, pH 3.5 - 4

PRO I 162515-68-6

RX(4) RCT I 162515-68-6

STAGE(1)

RGT J 1310-73-2 NaOH
 SOL 68-12-2 DMF, 7732-18-5 Water
 CON 10 minutes, room temperature

STAGE(2)

RCT N 920739-17-9
 SOL 109-99-9 THF
 CON 2 hours, 25 deg C

STAGE(3)

RCT O 108-91-8
 SOL 141-78-6 AcOEt
 CON 25 deg C

PRO P 945934-73-6

RX(9) OF 10 COMPOSED OF RX(2), RX(3), RX(4)

L3 ANSWER 6 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

SOL 67-64-1 Me2CO
 CON SUBSTAGE(1) 12 hours, room temperature -> reflux
 SUBSTAGE(2) reflux -> -3 deg C
 SUBSTAGE(3) 1 hour

RX(3) RCT G 945934-74-7

STAGE(1)

RGT J 1310-73-2 NaOH
 SOL 7732-18-5 Water
 CON SUBSTAGE(1) 14 hours, room temperature -> reflux
 SUBSTAGE(2) reflux -> room temperature

STAGE(2)

RGT K 64-18-6 HCO2H
 SOL 141-78-6 AcOEt
 CON -5 - 5 deg C, pH 3.5 - 4

PRO I 162515-68-6

RX(4) RCT I 162515-68-6

STAGE(1)

RGT J 1310-73-2 NaOH
 SOL 68-12-2 DMF, 7732-18-5 Water
 CON 10 minutes, room temperature

STAGE(2)

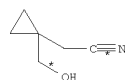
RCT N 920739-17-9
 SOL 109-99-9 THF
 CON 2 hours, 25 deg C

STAGE(3)

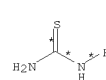
RCT O 108-91-8
 SOL 141-78-6 AcOEt
 CON 25 deg C

PRO P 945934-73-6

RX(10) OF 10 COMPOSED OF RX(1), RX(2), RX(3), RX(4)
 RX(10) A + F + N + O ==> P



A

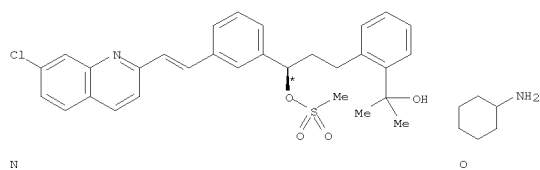


F

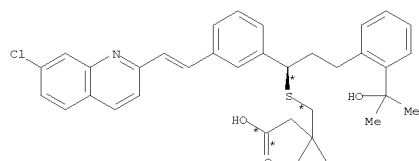
02/18/2009

10-576,971.trn

L3 ANSWER 6 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



4
STEPS
P: CM 1
YIELD 65%



P: CM 2
YIELD 65%

RX(1)

STAGE(1)
RGT C 7726-95-6 Br2, D 603-35-0 PPh3
SOL 75-05-8 MeCN
CON SUBSTAGE(1) room temperature -> -8 deg C
SUBSTAGE(2) -10 - 0 deg C
SUBSTAGE(3) 0 - 5 deg C

STAGE(2)

L3 ANSWER 7 OF 16 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 147:95564 CASREACT
TITLE: Process for preparation of montelukast sodium
INVENTOR(S): Chawla, Harmander Pal Singh; Chowdhary, Anil Shankar;
Patel, Ajay Mangubhai; Joshi, Vipul Narbhashankar;
Patel, Manish Popatlal
PATENT ASSIGNEE(S): Glade Organics Private Limited, India
SOURCE: PCT Int. Appl., 21pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007072114	A1	20070628	WO 2006-IB59	20060116
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, KG, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM			
IN 2005MU1613	A	20070706	IN 2005-MU1613	20051223
CA 2632954	A1	20070628	CA 2006-2632954	20060116
EP 1968942	A1	20080917	EP 2006-710236	20060116
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR			
PRIORITY APPLN. INFO.:			IN 2005-MU1613	20051223
			WO 2006-IB59	20060116

OTHER SOURCE(S): MARPAT 147:95564
AB This invention pertains to an improved process for the preparation of 1-[[[(1R)-1-[3-[(1E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl] cyclopropane acetic acid sodium salt (montelukast sodium). The title process consists of converting 1-(mercaptomethyl)-cyclopropaneacetic acid to a quaternary ammonium salt, then treating the salt with Bu lithium to provide an intermediate. Subsequent condensation of the intermediate with 2-[2-[(3S)-3-[3-[(E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[(methanesulfonyl)oxy]propyl]phenyl]-2-propanol afforded a quaternary ammonium salt of montelukast, which was then treated with sodium methoxide to generate montelukast sodium. The invention provides a convenient process for preparing montelukast sodium in good yields and purity.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

RX(1) OF 4 A + B + C ==> D...

L3 ANSWER 6 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

RCT A 152922-71-9
CON SUBSTAGE(1) <10 deg C
SUBSTAGE(2) 15 - 20 minutes, <10 deg C -> 60 deg C
SUBSTAGE(3) 1 hour, 60 deg C -> <-10 deg C

PRO B 338392-48-6

RX(2) RCT B 338392-48-6, F 62-56-6
PRO G 945934-74-7
SOL 67-64-1 Me2CO
CON SUBSTAGE(1) 12 hours, room temperature -> reflux
SUBSTAGE(2) reflux -> -3 deg C
SUBSTAGE(3) 1 hour

RX(3) RCT G 945934-74-7

STAGE(1)
RGT J 1310-73-2 NaOH
SOL 7732-18-5 Water
CON SUBSTAGE(1) 14 hours, room temperature -> reflux
SUBSTAGE(2) reflux -> room temperature

STAGE(2)
RGT K 64-18-6 HCO2H
SOL 141-78-6 AcOEt
CON -5 - 5 deg C, pH 3.5 - 4

PRO I 162515-68-6

RX(4) RCT I 162515-68-6

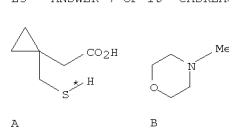
STAGE(1)
RGT J 1310-73-2 NaOH
SOL 68-12-2 DMF, 7732-18-5 Water
CON 10 minutes, room temperature

STAGE(2)
RCT N 920739-17-9
SOL 109-99-9 THF
CON 2 hours, 25 deg C

STAGE(3)
RCT O 108-91-8
SOL 141-78-6 AcOEt
CON 25 deg C

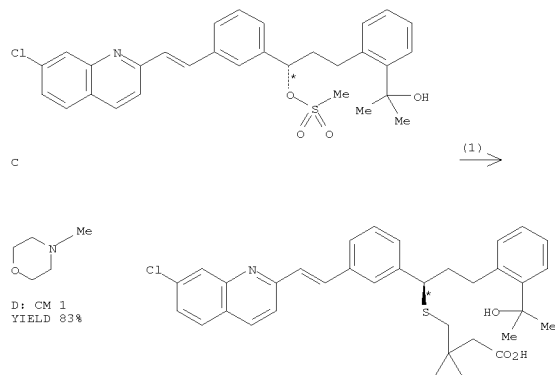
PRO P 945934-73-6

L3 ANSWER 7 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



A

B



C

D: CM 1
YIELD 83%

D: CM 2
YIELD 83%

RX(1) RCT A 162515-68-6, B 109-02-4

STAGE(1)
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, 25 deg C
SUBSTAGE(2) 25 deg C -> -40 deg C

STAGE(2)
RGT E 109-72-8 BuLi
CON 30 minutes, -40 - -20 deg C

STAGE(3)
RCT C 807638-71-7
SOL 109-99-9 THF
CON 12 hours, -10 - -5 deg C

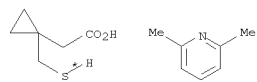
02/18/2009

10-576,971.trn

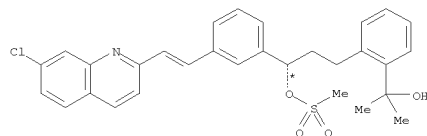
L3 ANSWER 7 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

PRO D 942303-96-0
NTE alternative preparation shown

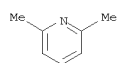
RX(3) OF 4 A + J + C ==> K



A J



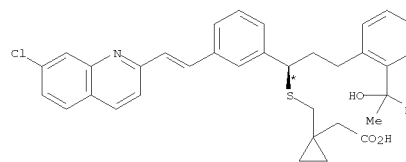
C



K: CM 1

(3)

L3 ANSWER 7 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



K: CM 2

RX(3) RCT A 162515-68-6, J 108-48-5

STAGE(1)

SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, 25 deg C
SUBSTAGE(2) 25 deg C -> -40 deg C

STAGE(2)

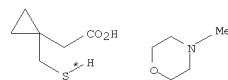
RGT E 109-72-8 BuLi
CON 30 minutes, -40 - -20 deg C

STAGE(3)

RCT C 807638-71-7
SOL 109-99-9 THF
CON 12 hours, -10 - -5 deg C

PRO K 942303-98-2
NTE alternative preparation shown

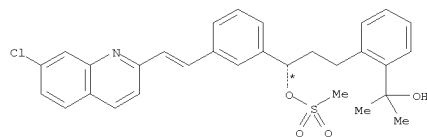
RX(4) OF 4 COMPOSED OF RX(1), RX(2)
RX(4) A + B + C ==> G



A

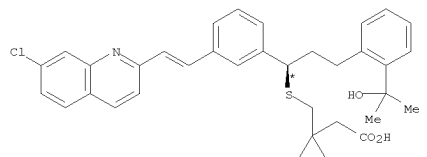
B

L3 ANSWER 7 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



C

2 STEPS



● Na

G
YIELD 90%

RX(1) RCT A 162515-68-6, B 109-02-4

STAGE(1)

SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, 25 deg C
SUBSTAGE(2) 25 deg C -> -40 deg C

STAGE(2)

RGT E 109-72-8 BuLi
CON 30 minutes, -40 - -20 deg C

STAGE(3)

RCT C 807638-71-7
SOL 109-99-9 THF
CON 12 hours, -10 - -5 deg C

PRO D 942303-96-0
NTE alternative preparation shown

RX(2) RCT D 942303-96-0
RGT H 124-41-4 NaOMe

L3 ANSWER 7 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

PRO G 151767-02-1
SOL 108-88-3 PhMe
CON 30 minutes, 25 - 30 deg C

02/18/2009

10-576,971.trn

L3 ANSWER 8 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 147:72655 CASREACT
 TITLE: Process for the preparation of Montelukast sodium
 from

(S)-benzenepropanol
 α -[3-[(1E)-2-(7-chloro-2-

quinolinyl)ethenyl]phenyl]-2-(1-hydroxy-1-methylethyl)-
 , 1-methanesulfonate with
 1-(mercaptomethyl)cyclopropanecetic acid in the
 presence of strong bases in polar aprotic solvents.

INVENTOR(S): Satyanarayana, Reddy Manne; Kihore, Kumar Muppa;
 Thirumalai, Rajan Srinivasan; Ramasubba, Reddy
 Karamala

PATENT ASSIGNEE(S): MSN Laboratories Limited, India
 SOURCE: PCT Int. Appl., 39pp.

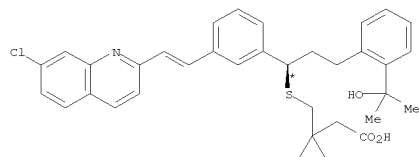
DOCUMENT TYPE: Patent
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007069261	A1	20070621	WO 2006-IN86	20060310
<p>W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW</p> <p>RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM</p> <p>IN 2005CH01818 A 20070831 IN 2005-CH1818 20051213 EP 1968943 A1 20080917 EP 2006-728408 20060310</p> <p>R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR</p> <p>PRIORITY APPLN. INFO.: IN 2005-CH1818 20051213 WO 2006-IN86 20060310</p>				

AB A process for the preparation of Montelukast and its pharmaceutically acceptable salts comprises reaction of (S)-benzenepropanol α -[3-[(1E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-2-(1-hydroxy-1-methylethyl)-, 1-methanesulfonate with 1-(mercaptomethyl)cyclopropanecetic acid in the presence of strong bases in polar aprotic solvents and C1-4 alcs. at -20° to 0° for 5-20 h followed by quenching the reaction, lowering the pH with HOAc, extracting the Montelukast, treating the product with organic amines, optionally purifying the montelukast amine salt, and converting the amine salt to the Na salt using NaOMe.

L3 ANSWER 8 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



D: CM 2

RX(1)

STAGE(1)
 RGT E 67-68-5 DMSO, F 124-41-4 NaOMe
 SOL 67-56-1 MeOH
 CON room temperature -> 0 deg C

STAGE(2)
 RCT A 162515-68-6
 CON 60 minutes, -5 - 0 deg C

STAGE(3)
 RCT B 920739-17-9
 CON SUBSTAGE(1) -5 - 0 deg C
 SUBSTAGE(2) 10 hours, -5 - 5 deg C

STAGE(4)
 SOL 7732-18-5 Water
 CON 30 minutes, 10 - 20 deg C

STAGE(5)
 RGT G 1310-73-2 NaOH
 SOL 7732-18-5 Water
 CON 10 - 20 deg C

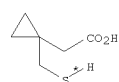
STAGE(6)
 RCT C 101-83-7
 SOL 141-78-6 AcOEt
 CON 10 hours, 25 - 35 deg C

PRO D 577953-88-9
 NTE alternative preparation shown

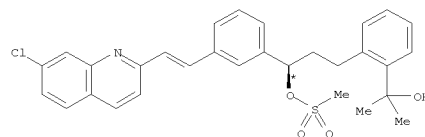
RX(3) OF 3 COMPOSED OF RX(1), RX(2)
 RX(3) A + B + C ==> K

L3 ANSWER 8 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)
 REFERENCE COUNT: 2
 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

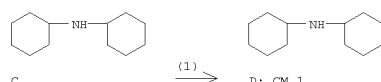
RX(1) OF 3 A + B + C ==> D...



A



B

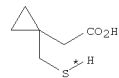


C

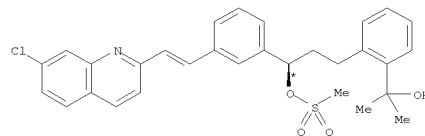
(1)

D: CM 1

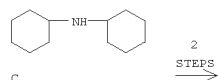
L3 ANSWER 8 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



A



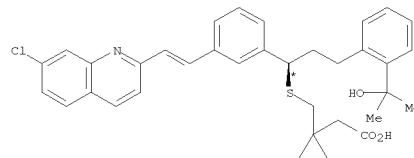
B



C

2

STEPS



Na

K

RX(1)

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L3 ANSWER 8 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

STAGE(1)

RGT E 67-68-5 DMSO, F 124-41-4 NaOMe
 SOL 67-56-1 MeOH
 CON room temperature -> 0 deg C

STAGE(2)

RCT A 162515-68-6
 CON 60 minutes, -5 - 0 deg C

STAGE(3)

RCT B 920739-17-9
 CON SUBSTAGE(1) -5 - 0 deg C
 SUBSTAGE(2) 10 hours, -5 - 5 deg C

STAGE(4)

SOL 7732-18-5 Water
 CON 30 minutes, 10 - 20 deg C

STAGE(5)

RGT G 1310-73-2 NaOH
 SOL 7732-18-5 Water
 CON 10 - 20 deg C

STAGE(6)

RCT C 101-83-7
 SOL 141-78-6 AcOEt
 CON 10 hours, 25 - 35 deg C

PRO D 577953-88-9

NTE alternative preparation shown

RX(2)

RCT D 577953-88-9
 RGT F 124-41-4 NaOMe
 PRO K 151767-02-1
 SOL 67-56-1 MeOH
 CON 60 minutes, 25 - 35 deg C

L3 ANSWER 9 OF 16 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:

146:142518 CASREACT

TITLE:

Purification of montelukast

INVENTOR(S):

Sterimbaum, Greta; Shapiro, Evgeny; Chen, Kobi

PATENT ASSIGNEE(S):

Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceutical Usa, Inc.

SOURCE:

PCT Int. Appl., 34pp.

CODEN: PIXKD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

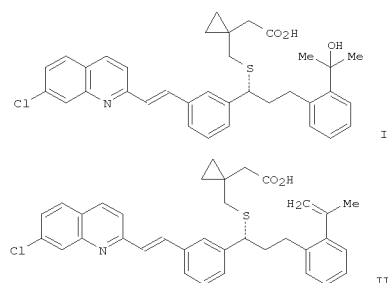
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007005965	A1	20070111	WO 2006-US26192	20060705
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
CA 2608369	A1	20070111	CA 2006-2608369	20060705
US 20070078158	A1	20070405	US 2006-481877	20060705
EP 1904448	A1	20080402	EP 2006-786369	20060705
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR			
JP 2008510840	T	20080410	JP 2007-530514	20060705
MX 2007002609	A	20080828	MX 2007-2609	20070301
KR 2007088504	A	20070829	KR 2007-705247	20070305
IN 2007DN09336	A	20080111	IN 2007-DN9336	20071204
CN 101213177	A	20080702	CN 2006-80024298	20080102
KR 2009015186	A	20090211	KR 2009-700703	20090113
PRIORITY APPLN. INFO.:			US 2005-697000P	20050705
			WO 2006-US26192	20060705
			KR 2007-705247	20070305

GI

L3 ANSWER 9 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

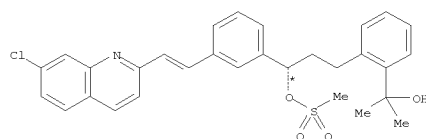


AB The present invention provides methods of purifying montelukast (I), a new isolated impurity of montelukast of formula (II), method for its isolation, and method of using montelukast impurity as a reference marker and a reference standard A process for preparing pure montelukast sodium salt comprises (1) providing a montelukast free acid, (2) converting the montelukast free acid to the di-n-propylamine montelukast salt, (3) and converting the di-n-propylamine montelukast salt to montelukast sodium salt. The impurity is used as a reference marker for determination of the purity of montelukast by HPLC or TLC.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

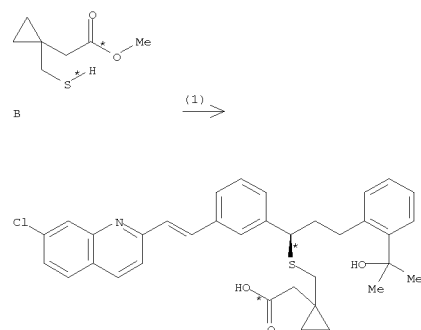
FORMAT

RX(1) OF 13 A + B ==> C...



A

L3 ANSWER 9 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



C

RX(1) RCT A 807638-71-7, B 152922-73-1

STAGE(1)

RGT D 1310-73-2 NaOH
 SOL 7732-18-5 Water, 127-19-5 AcNMe2
 CON SUBSTAGE(1) 9 minutes, -7 deg C
 SUBSTAGE(2) -7 deg C -> -1 deg C
 SUBSTAGE(3) 1 hour, -6 deg C
 SUBSTAGE(4) 1.5 hours, 18 deg C
 SUBSTAGE(5) 18 deg C -> 38 deg C
 SUBSTAGE(6) 1 hour, 38 deg C

STAGE(2)

RGT D 1310-73-2 NaOH
 SOL 7732-18-5 Water
 CON overnight, 38 deg C

STAGE(3)

RGT E 7647-14-5 NaCl
 SOL 7732-18-5 Water

STAGE(4)

RGT F 87-69-4 L-(+)-Tartaric acid
 SOL 109-99-9 THF
 CON pH 3 - 5

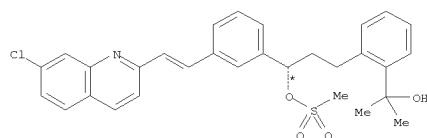
PRO C 158966-92-8

RX(6) OF 13 COMPOSED OF RX(1), RX(2)

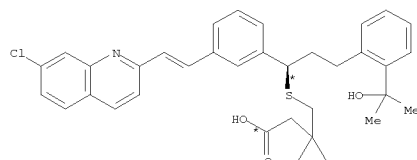
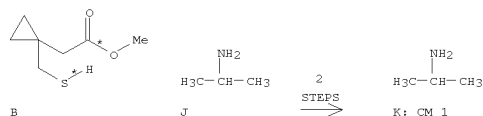
02/18/2009

10-576,971.trn

L3 ANSWER 9 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)
 RX(6) A + B + J ==> K



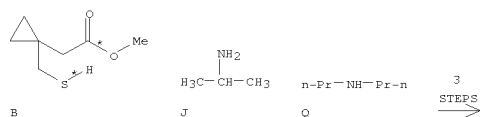
A



K: CM 2

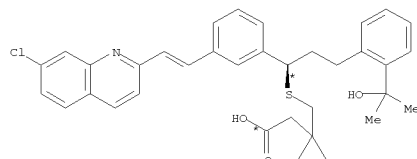
RX(1) RCT A 807638-71-7, B 152922-73-1
 STAGE(1)
 RGT D 1310-73-2 NaOH
 SOL 7732-18-5 Water, 127-19-5 AcNMe2
 CON SUBSTAGE(1) 9 minutes, -7 deg C
 SUBSTAGE(2) -7 deg C -> -1 deg C
 SUBSTAGE(3) 1 hour, -6 deg C
 SUBSTAGE(4) 1.5 hours, 18 deg C

L3 ANSWER 9 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



n-Pr-NH-Pr-n

R: CM 1



R: CM 2

RX(1) RCT A 807638-71-7, B 152922-73-1
 STAGE(1)
 RGT D 1310-73-2 NaOH
 SOL 7732-18-5 Water, 127-19-5 AcNMe2
 CON SUBSTAGE(1) 9 minutes, -7 deg C
 SUBSTAGE(2) -7 deg C -> -1 deg C
 SUBSTAGE(3) 1 hour, -6 deg C
 SUBSTAGE(4) 1.5 hours, 18 deg C
 SUBSTAGE(5) 18 deg C -> 38 deg C
 SUBSTAGE(6) 1 hour, 38 deg C
 STAGE(2)
 RGT D 1310-73-2 NaOH
 SOL 7732-18-5 Water
 CON overnight, 38 deg C
 STAGE(3)
 RGT E 7647-14-5 NaCl
 SOL 7732-18-5 Water
 STAGE(4)
 RGT F 87-69-4 L-(+)-Tartaric acid
 SOL 109-99-9 THF

L3 ANSWER 9 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)
 SUBSTAGE(5) 18 deg C -> 38 deg C
 SUBSTAGE(6) 1 hour, 38 deg C

STAGE(2)
 RGT D 1310-73-2 NaOH
 SOL 7732-18-5 Water
 CON overnight, 38 deg C

STAGE(3)
 RGT E 7647-14-5 NaCl
 SOL 7732-18-5 Water

STAGE(4)
 RGT F 87-69-4 L-(+)-Tartaric acid
 SOL 109-99-9 THF
 CON pH 3 - 5

PRO C 158966-92-8

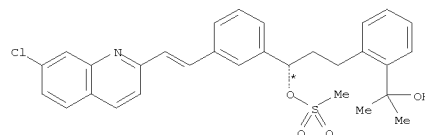
RX(2) RCT C 158966-92-8, J 75-31-0

STAGE(1)
 CON SUBSTAGE(1) 0.5 hours, room temperature
 SUBSTAGE(2) 55 deg C, 20 mbar

STAGE(2)
 RGT L 78-93-3 EtCOMe
 CON 50 deg C

PRO K 918972-53-9

RX(10) OF 13 COMPOSED OF RX(1), RX(2), RX(4)
 RX(10) A + B + J + Q ==> R



A

L3 ANSWER 9 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)
 CON pH 3 - 5

PRO C 158966-92-8

RX(2) RCT C 158966-92-8, J 75-31-0

STAGE(1)
 CON SUBSTAGE(1) 0.5 hours, room temperature
 SUBSTAGE(2) 55 deg C, 20 mbar

STAGE(2)
 RGT L 78-93-3 EtCOMe
 CON 50 deg C

PRO K 918972-53-9

RX(4) RCT K 918972-53-9

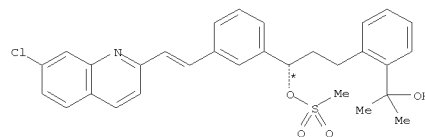
STAGE(1)
 RGT S 64-19-7 AcOH
 SOL 109-99-9 THF, 108-88-3 PhMe
 CON 40 minutes, room temperature, pH 5 - 6

STAGE(2)
 RCT Q 142-84-7
 CON 0.5 hours, room temperature

STAGE(3)
 RGT T 108-88-3 PhMe
 CON SUBSTAGE(1) 40 deg C
 SUBSTAGE(2) 40 deg C -> 25 deg C
 SUBSTAGE(3) 0.5 hours, 25 deg C
 SUBSTAGE(4) 25 deg C -> 0 deg C
 SUBSTAGE(5) overnight, 0 deg C

PRO R 880769-26-6

RX(13) OF 13 COMPOSED OF RX(1), RX(2), RX(4), RX(5)
 RX(13) A + B + J + Q ==> U

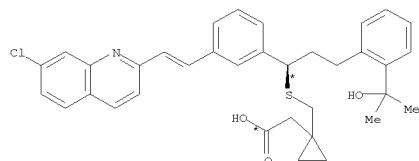
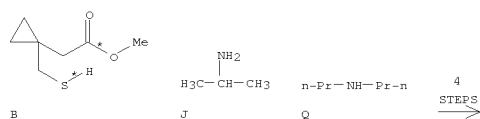


A

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L3 ANSWER 9 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



U

RX(1) RCT A 807638-71-7, B 152922-73-1

STAGE(1)

RGT D 1310-73-2 NaOH

SOL 7732-18-5 Water, 127-19-5 AcNMe2

CON SUBSTAGE(1) 9 minutes, -7 deg C

SUBSTAGE(2) -7 deg C -> -1 deg C

SUBSTAGE(3) 1 hour, -6 deg C

SUBSTAGE(4) 1.5 hours, 18 deg C

SUBSTAGE(5) 18 deg C -> 38 deg C

SUBSTAGE(6) 1 hour, 38 deg C

STAGE(2)

RGT D 1310-73-2 NaOH

SOL 7732-18-5 Water

CON overnight, 38 deg C

STAGE(3)

RGT E 7647-14-5 NaCl

SOL 7732-18-5 Water

L3 ANSWER 10 OF 16 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 145:83245 CASREACT

TITLE: Preparation of salts of the leukotriene antagonist montelukast

INVENTOR(S): Srinivas, Pathi L.; Rao, Dharmaraj Ramachandra; Kankan, Rajendra Narayanrao; Relekar, Jayamadhava P.

PATENT ASSIGNEE(S): Cipla Limited, India

SOURCE: PCT Int. Appl., 17 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006064269	A2	20060622	WO 2005-GB4896	20051216
WO 2006064269	A3	20060928		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

IN 2004MU01357 A 20060721 IN 2004-MU1357 20041217

PRIORITY APPLN. INFO.: IN 2004-MU1357 20041217

AB Claimed is an alkaline earth metal salt of montelukast. Also claimed is a

process for preparing an alkali or alkaline earth metal salt of montelukast.

Thus, 1-(mercaptomethyl)cyclopropanecarboxylic acid in DMSO was treated with sodium hydride; a solution of 2-(2-(2(S)-(3-(2-(7-chloro-2-quinolinyl)ethenyl)phenyl)-3-methanesulfonyloxypropyl)phenyl)-2-propanol in THF and DMSO was added over 1.5 h; the reaction mixture was stirred

at 0 to -5°C for 1 h; acetic acid was added to the reaction mixture with stirring; after addition of water, the reaction mixture was extracted with Et acetate; the Et acetate layer was dried and distilled to give a residue which

was dissolved in methanol and treated with charcoal and filtered to give a

filtrate which was mixed with a solution of magnesium chloride in Et alc.; the resulting mixture was distilled to give a residue which was mixed

with toluene; heptane was then added slowly to the mixture over 3 to 4 h to give

the magnesium salt of montelukast.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L3 ANSWER 9 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

STAGE(4)

RGT F 87-69-4 L-(+)-Tartaric acid

SOL 109-99-9 THF

CON pH 3 - 5

PRO C 158966-92-8

RX(2) RCT C 158966-92-8, J 75-31-0

STAGE(1)

CON SUBSTAGE(1) 0.5 hours, room temperature

SUBSTAGE(2) 55 deg C, 20 mbar

STAGE(2)

RGT L 78-93-3 EtCOMe

CON 50 deg C

PRO K 918972-53-9

RX(4) RCT K 918972-53-9

STAGE(1)

RGT S 64-19-7 AcOH

SOL 109-99-9 THF, 108-88-3 PhMe

CON 40 minutes, room temperature, pH 5 - 6

STAGE(2)

RCT Q 142-84-7

CON 0.5 hours, room temperature

STAGE(3)

RGT T 108-88-3 PhMe

CON SUBSTAGE(1) 40 deg C

SUBSTAGE(2) 40 deg C -> 25 deg C

SUBSTAGE(3) 0.5 hours, 25 deg C

SUBSTAGE(4) 25 deg C -> 0 deg C

SUBSTAGE(5) overnight, 0 deg C

PRO R 880769-26-6

RX(5) RCT R 880769-26-6

RGT V 865-48-5 NaOBu-t

PRO U 151767-02-1

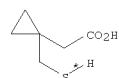
SOL 108-88-3 PhMe

CON SUBSTAGE(1) 30 minutes, room temperature

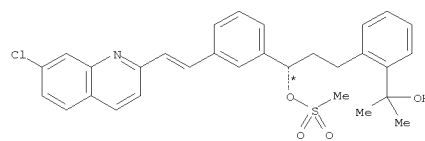
SUBSTAGE(2) 30 minutes, 30 - 40 deg C

L3 ANSWER 10 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

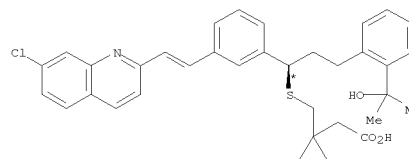
RX(1) OF 4 A + B ==> C



A



B



1/2 Mg

C

RX(1) RCT A 162515-68-6

STAGE(1)

RGT D 7646-69-7 NaH

SOL 67-68-5 DMSO

CON 30 minutes, -5 - 0 deg C

STAGE(2)

RCT B 807638-71-7

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L3 ANSWER 10 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)
 SOL 109-99-9 THF, 67-68-5 DMSO
 CON SUBSTAGE(1) 1.5 hours, -5 - 0 deg C
 SUBSTAGE(2) 1 hour, 0 - 5 deg C

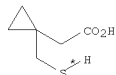
STAGE(3)
 RGT E 7732-18-5 Water, F 64-19-7 AcOH
 CON 30 minutes, -5 - 0 deg C

STAGE(4)
 RGT G 7786-30-3 MgCl2
 SOL 67-56-1 MeOH, 141-78-6 AcOEt
 CON 30 minutes, 25 - 30 deg C

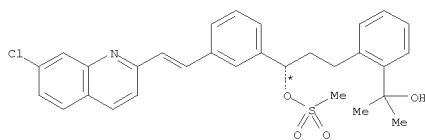
STAGE(5)
 SOL 108-20-3 Isopropyl ether
 CON cooled

PRO C 577953-86-7
 NTE stereoselective

RX(2) OF 4 A + B ==> C



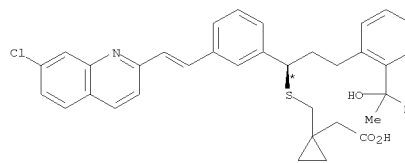
A



B



L3 ANSWER 10 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



● 1/2 Mg

C

RX(2) RCT A 162515-68-6

STAGE(1)
 RGT M 109-72-8 BuLi
 SOL 109-99-9 THF
 CON 2 hours, -15 - -10 deg C

STAGE(2)
 RCT B 807638-71-7
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 2 hours, -5 - 0 deg C
 SUBSTAGE(2) 15 hours, -5 - 0 deg C

STAGE(3)
 RGT N 7647-14-5 NaCl
 SOL 7732-18-5 Water
 CON <0 deg C

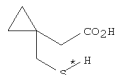
STAGE(4)
 RGT G 7786-30-3 MgCl2
 SOL 67-56-1 MeOH, 141-78-6 AcOEt
 CON 30 minutes, 25 - 30 deg C

STAGE(5)
 SOL 108-20-3 Isopropyl ether
 CON cooled

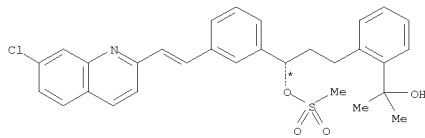
PRO C 577953-86-7
 NTE stereoselective

RX(3) OF 4 A + B ==> O

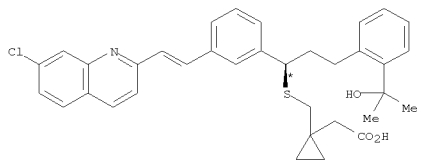
L3 ANSWER 10 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



A



B



● 1/2 Ca

O

RX(3) RCT A 162515-68-6

STAGE(1)
 RGT M 109-72-8 BuLi
 SOL 109-99-9 THF
 CON 2 hours, -15 - -10 deg C

STAGE(2)
 RCT B 807638-71-7
 SOL 109-99-9 THF

L3 ANSWER 10 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)
 CON SUBSTAGE(1) 2 hours, -5 - 0 deg C
 SUBSTAGE(2) 15 hours, -5 - 0 deg C

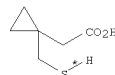
STAGE(3)
 RGT N 7647-14-5 NaCl
 SOL 7732-18-5 Water
 CON <0 deg C

STAGE(4)
 RGT P 10043-52-4 CaCl2
 SOL 67-56-1 MeOH, 141-78-6 AcOEt
 CON 30 minutes, 25 - 30 deg C

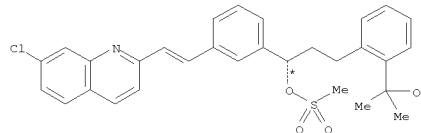
STAGE(5)
 SOL 108-20-3 Isopropyl ether
 CON cooled

PRO O 577953-85-6
 NTE stereoselective

RX(4) OF 4 A + B ==> Q



A



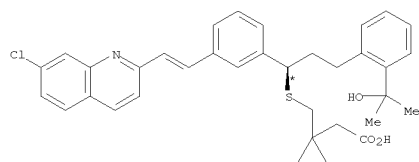
B



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L3 ANSWER 10 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



Q
alkali metal s
alts

RX(4) RCT A 162515-68-6

STAGE(1)

RGT D 7646-69-7 NaH
SOL 67-68-5 DMSO
CON 30 minutes, -5 - 0 deg C

STAGE(2)

RGT B 807638-71-7
SOL 109-99-9 THF, 67-68-5 DMSO
CON SUBSTAGE(1) 1.5 hours, -5 - 0 deg C
SUBSTAGE(2) 1 hour, 0 - 5 deg C

STAGE(3)

RGT E 7732-18-5 Water, F 64-19-7 AcOH
CON 30 minutes, -5 - 0 deg C

STAGE(4)

RGT P 10043-52-4 CaCl₂
SOL 67-56-1 MeOH, 141-78-6 AcOEt
CON 30 minutes, 25 - 30 deg C

STAGE(5)

SOL 108-20-3 Isopropyl ether
CON cooled

PRO Q 158966-92-8D
NTE stereoselective

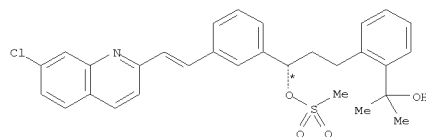
L3 ANSWER 11 OF 16 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 145:45965 CASREACT
TITLE: Process for preparation of montelukast sodium as
leukotriene antagonists
INVENTOR(S): Chamorro Gutierrez, Iolanda; Bosch i Llado, Jordi;
Molins i Grau, Elies
PATENT ASSIGNEE(S): Medichem, S.A., Spain
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006058545	A1	20060608	WO 2004-EP13598	20041130
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
CA 2589936	A1	20060608	CA 2004-2589936	20041130
EP 1817289	A1	20070815	EP 2004-798127	20041130
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR			
IN 2007KN01950	A	20070810	IN 2007-KN1950	20070530
US 20080214822	A1	20080904	US 2007-791896	20070824
PRIORITY APPLN. INFO.:			WO 2004-EP13598	20041130
AB	The present invention provides a process for the preparation of montelukast sodium and precursors thereof as leukotriene antagonists (no data). For example, (1S)-[3-[(1E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-2-[(1-hydroxy-1-methylethyl)benzenepropanol was reacted with methanesulfonyl chloride in THF to give the mesylate intermediate. The mesylate obtained in the previous step was reacted with [1-(mercaptomethyl)cyclopropyl]acetic acid in DMF in the presence of sodium hydroxide, followed by acidifying and treating with one equivalent NaOH in ethanol to give montelukast sodium with high purity.			
REFERENCE COUNT:	5	THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE		
FORMAT				

RX(2) OF 5 ...C + G ==> H

L3 ANSWER 11 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

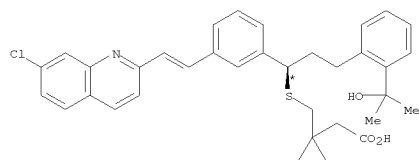


C



G

(2) →



H
YIELD 71%

RX(2) RCT C 807638-71-7, G 162515-68-6

STAGE(1)

RGT I 1310-73-2 NaOH
SOL 68-12-2 DMF
CON 6 hours, -5 - 0 deg C

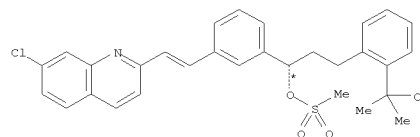
STAGE(2)

RGT J 7647-14-5 NaCl
SOL 7732-18-5 Water, 108-21-4 Acetic acid, 1-methylethyl ester
CON 15 minutes, heated

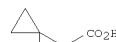
PRO H 158966-92-8
NTE small exotherm stage 2, author shows purification, optimization

L3 ANSWER 11 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

RX(3) OF 5 ...C + G ==> N

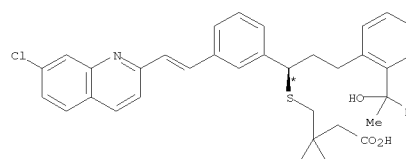


C



G

(3) →



● Na

N

RX(3) RCT C 807638-71-7, G 162515-68-6

STAGE(1)

RGT I 1310-73-2 NaOH
SOL 68-12-2 DMF
CON 6 hours, -5 - 0 deg C

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L3 ANSWER 11 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

STAGE(2)
 RGT J 7647-14-5 NaCl
 SOL 7732-18-5 Water, 108-21-4 Acetic acid, 1-methylethyl ester
 CON 15 minutes, heated

STAGE(3)
 RGT I 1310-73-2 NaOH
 SOL 7732-18-5 Water, 64-17-5 EtOH

PRO N 151767-02-1
 NTE small exotherm stage 2, author shows purification, optimization study, scalable, stereoselective

L3 ANSWER 12 OF 16 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 143:386935 CASREACT
 TITLE: Process for the preparation of
 [R-(E)-1-[[[1-[3-[2-[7-chloro-2-quinolinyl]ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]cyclopropaneacetic acid (montelukast) and its pharmaceutically acceptable salts

INVENTOR(S): Sundaram, Venkataraman; Rajan, Srinivasan Thirumalai; Bulusu, Veera Venkata Naga Chandria Sekhar; Srivastav, Alokumar; Kasturi, Ravi Kumar; Aavula, Sanjeev Kumar

PATENT ASSIGNEE(S): India

SOURCE: U.S. Pat. Appl. Publ., 7 pp.
 CODEN: USXXCO

DOCUMENT TYPE: Patent
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050234241	A1	20051020	US 2004-932562	20040902
US 7189853	B2	20070313		
IN 2004CH00342	A	20070914	IN 2004-CH342	20040415
PRIORITY APPLN. INFO.:			IN 2004-CH342	20040415

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

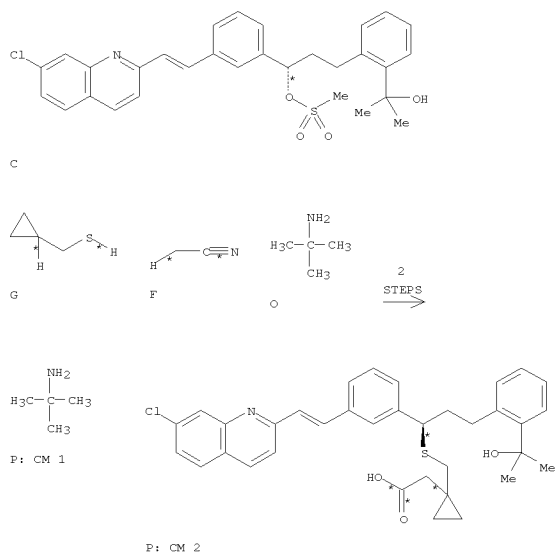
AB The present invention is related to a process for preparing montelukast (I) involving substitution of II (preparation given) with an alkali salt of a compound of formula III (wherein X=CN or CONH2) followed by hydrolysis.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

RX(13) OF 31 COMPOSED OF RX(2), RX(3)
 RX(13) C + G + F + O ==> P

L3 ANSWER 12 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



RX(2) RCT C 807638-71-7, G 5617-79-8, F 75-05-8

STAGE(1)
 RGT I 109-72-8 BuLi
 SOL 68-12-2 DMF, 110-54-3 Hexane
 CON 6 - 8 hours, -15 - -10 deg C

STAGE(2)
 RGT J 7647-14-5 NaCl
 SOL 108-88-3 PhMe, 7732-18-5 Water
 CON 20 minutes

STAGE(3)
 SOL 7732-18-5 Water, 64-19-7 AcOH
 CON 30 - 40 minutes, 25 - 35 deg C

L3 ANSWER 12 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

PRO H 866923-62-8
 NTE stereoselective

RX(3) RCT H 866923-62-8

STAGE(1)
 CON 6 - 8 hours, 118 - 122 deg C

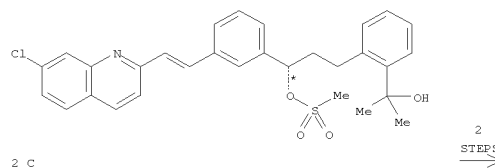
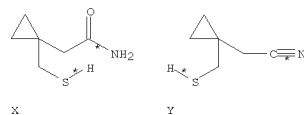
STAGE(2)
 SOL 108-88-3 PhMe, 7732-18-5 Water
 CON 20 - 30 minutes, 90 deg C

STAGE(3)
 RGT N 64-19-7 AcOH
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 25 - 35 deg C, pH 4.8 - 5

STAGE(4)
 RCT O 75-64-9
 SOL 67-64-1 Me2CO
 CON 8 - 10 hours, 25 - 35 deg C

PRO P 851755-58-3
 NTE caustic lye added stage 1

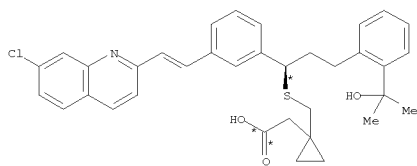
RX(15) OF 31 COMPOSED OF RX(6), RX(7)
 RX(15) X + Y + 2 C ==> AA



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L3 ANSWER 12 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



AA

RX(6) RCT X 162515-69-7, Y 866923-64-0

STAGE(1)

RGT I 109-72-8 BuLi
 SOL 68-12-2 DMF, 110-54-3 Hexane
 CON 20 minutes, <0 deg C

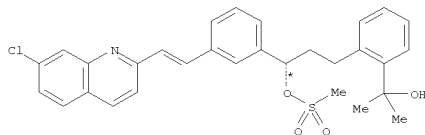
STAGE(2)

RCT C 807638-71-7
 CON 5 hours, <0 deg C

PRO Z 866923-63-9
 NTE stereoselective

RX(7) RCT Z 866923-63-9
 RGT S 1310-58-3 KOH
 PRO AA 158966-92-8
 SOL 111-46-6 (HOCH₂CH₂)₂O, 7732-18-5 Water
 CON 24 hours, reflux

RX(22) OF 31 COMPOSED OF RX(2), RX(3), RX(5)
 RX(22) C + G + F + O ==> U



C

L3 ANSWER 12 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

STAGE(1)

CON 6 - 8 hours, 118 - 122 deg C

STAGE(2)

SOL 108-88-3 PhMe, 7732-18-5 Water
 CON 20 - 30 minutes, 90 deg C

STAGE(3)

RGT N 64-19-7 AcOH
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 25 - 35 deg C, pH 4.8 - 5

STAGE(4)

RCT O 75-64-9
 SOL 67-64-1 Me₂CO
 CON 8 - 10 hours, 25 - 35 deg C

PRO P 851755-58-3
 NTE caustic lye added stage 1

RX(5) RCT P 851755-58-3

STAGE(1)

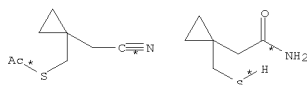
RGT N 64-19-7 AcOH
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 30 - 60 minutes, 25 - 35 deg C

STAGE(2)

RGT V 1310-73-2 NaOH
 SOL 67-56-1 MeOH
 CON 30 - 60 minutes, 25 - 35 deg C

PRO U 151767-02-1
 NTE work-up

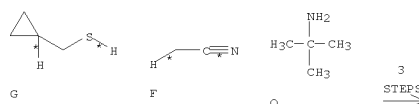
RX(24) OF 31 COMPOSED OF RX(9), RX(6), RX(7)
 RX(24) AB + X + 2 C ==> AA



AB

X

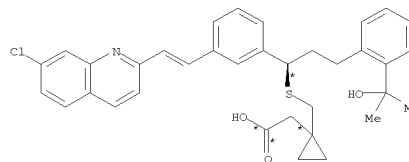
L3 ANSWER 12 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



G

F

O

3
STEPS

● Na

U

RX(2) RCT C 807638-71-7, G 5617-79-8, F 75-05-8

STAGE(1)

RGT I 109-72-8 BuLi
 SOL 68-12-2 DMF, 110-54-3 Hexane
 CON 6 - 8 hours, -15 - -10 deg C

STAGE(2)

RGT J 7647-14-5 NaCl
 SOL 108-88-3 PhMe, 7732-18-5 Water
 CON 20 minutes

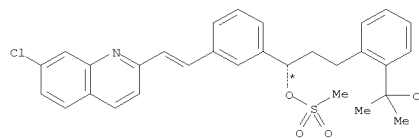
STAGE(3)

SOL 7732-18-5 Water, 64-19-7 AcOH
 CON 30 - 40 minutes, 25 - 35 deg C

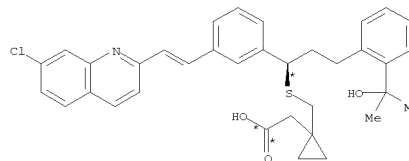
PRO H 866923-62-8
 NTE stereoselective

RX(3) RCT H 866923-62-8

L3 ANSWER 12 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



2 C

3
STEPS

AA

RX(9) RCT AB 152922-72-0

STAGE(1)

RGT AC 124-41-4 NaCMe
 SOL 67-56-1 MeOH
 CON -15 - -12 deg C

STAGE(2)

RGT N 64-19-7 AcOH
 SOL 7732-18-5 Water
 CON 20 - 30 minutes, <0 deg C, acidify

PRO Y 866923-64-0

RX(6) RCT X 162515-69-7, Y 866923-64-0

STAGE(1)

RGT I 109-72-8 BuLi
 SOL 68-12-2 DMF, 110-54-3 Hexane
 CON 20 minutes, <0 deg C

STAGE(2)

RCT C 807638-71-7
 CON 5 hours, <0 deg C

PRO Z 866923-63-9

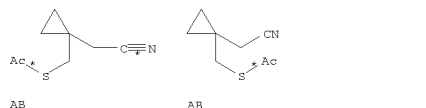
02/18/2009

10-576,971.trn

L3 ANSWER 12 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

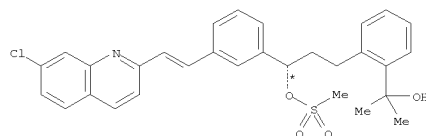
RX(7) RCT Z 866923-63-9
NTE stereoselective
RGT S 1310-58-3 KOH
PRO AA 158966-92-8
SOL 111-46-6 (HOCH₂CH₂)₂O, 7732-18-5 Water
CON 24 hours, reflux

RX(25) OF 31 COMPOSED OF RX(10), RX(6), RX(7)
RX(25) 2 AB + 2 C ==> AA

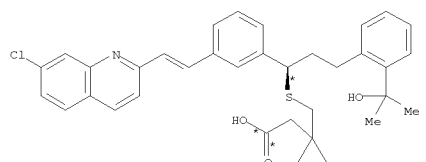


AB

AB

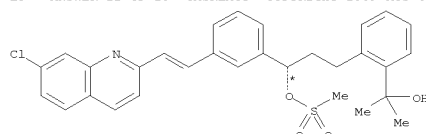


2 C

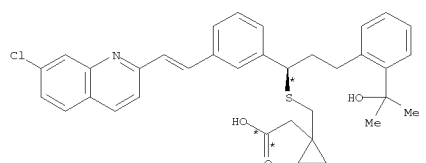
3
STEPS

AA

L3 ANSWER 12 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



2 C

3
STEPS

AA

RX(9) RCT AB 152922-72-0

STAGE(1)

RGT AC 124-41-4 NaOMe
SOL 67-56-1 MeOH
CON -15 - -12 deg C

STAGE(2)

RGT N 64-19-7 AcOH
SOL 7732-18-5 Water
CON 20 - 30 minutes, <0 deg C, acidify

PRO Y 866923-64-0

RX(10) RCT AB 152922-72-0
RGT S 1310-58-3 KOH
PRO X 162515-69-7, Y 866923-64-0
SOL 67-56-1 MeOH, 7732-18-5 Water
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) <50 deg C
NTE chemoselective, 3:2 acetamide:acetonitrile

RX(6) RCT X 162515-69-7, Y 866923-64-0

STAGE(1)

RGT I 109-72-8 BuLi
SOL 68-12-2 DMF, 110-54-3 Hexane

L3 ANSWER 12 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

RX(10) RCT AB 152922-72-0
RGT S 1310-58-3 KOH
PRO X 162515-69-7, Y 866923-64-0
SOL 67-56-1 MeOH, 7732-18-5 Water
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) <50 deg C
NTE chemoselective, 3:2 acetamide:acetonitrile

RX(6) RCT X 162515-69-7, Y 866923-64-0

STAGE(1)

RGT I 109-72-8 BuLi
SOL 68-12-2 DMF, 110-54-3 Hexane
CON 20 minutes, <0 deg C

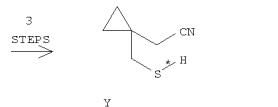
STAGE(2)

RCT C 807638-71-7
CON 5 hours, <0 deg C

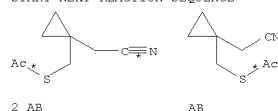
PRO Z 866923-63-9
NTE stereoselective

RX(7) RCT Z 866923-63-9
RGT S 1310-58-3 KOH
PRO AA 158966-92-8
SOL 111-46-6 (HOCH₂CH₂)₂O, 7732-18-5 Water
CON 24 hours, reflux

RX(30) OF 31 COMPOSED OF REACTION SEQUENCE RX(9), RX(6), RX(7)
AND REACTION SEQUENCE RX(10), RX(6), RX(7)
...AB ==> Y...
...2 AB + 2 C ==> AA



START NEXT REACTION SEQUENCE



2 AB

AB

L3 ANSWER 12 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

CON 20 minutes, <0 deg C

STAGE(2)

RCT C 807638-71-7
CON 5 hours, <0 deg C

PRO Z 866923-63-9
NTE stereoselective

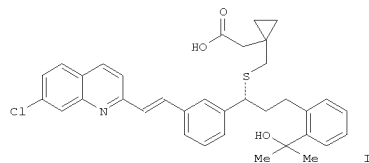
RX(7) RCT Z 866923-63-9
RGT S 1310-58-3 KOH
PRO AA 158966-92-8
SOL 111-46-6 (HOCH₂CH₂)₂O, 7732-18-5 Water
CON 24 hours, reflux

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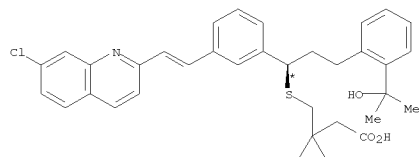
L3 ANSWER 13 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 142:38157 CASREACT
 TITLE: An improved method for preparation of montelukast acid
 and sodium salt
 INVENTOR(S): Suri, Sanjay; Singh, Jujhhar; Sarin, Gurdeep Singh;
 Tanwar, Madan Pal; Mahendru, Manu
 PATENT ASSIGNEE(S): Morepen Laboratories Limited, India
 SOURCE: PCT Int. Appl., 36 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108679	A1	20041216	WO 2003-IN214	20030606
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2528228	A1	20041216	CA 2003-2528228	20030606
AU 2003253247	A1	20050104	AU 2003-253247	20030606
EP 1631550	A1	20060308	EP 2003-817134	20030606
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK			
US 20070082925	A1	20070412	US 2006-576971	20060425
PRIORITY APPLN. INFO.:			WO 2003-IN214	20030606
GI				



AB The invention relates to a preparation of montelukast acid sodium salt of formula I•Na in amorphous form, useful as leukotriene antagonist (no biol. data). The method comprises of following steps: (a) generating the

L3 ANSWER 13 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



I: CM 2

RX(2) RCT G 162515-68-6

STAGE(1)

RGT J 109-72-8 BuLi
 SOL 109-99-9 THF, 110-54-3 Hexane
 CON SUBSTAGE(1) -15 - -10 deg C
 SUBSTAGE(2) 0.5 hours, -15 - -10 deg C

STAGE(2)

RCT C 807638-71-7
 SOL 109-99-9 THF
 CON SUBSTAGE(1) room temperature -> -5 deg C
 SUBSTAGE(2) -10 - -5 deg C
 SUBSTAGE(3) 0.25 hours, -10 - -5 deg C

STAGE(3)

SOL 109-99-9 THF
 CON SUBSTAGE(1) 0.5 hours, -7 - -3 deg C
 SUBSTAGE(2) 12 hours

STAGE(4)

RGT K 7647-14-5 NaCl
 SOL 7732-18-5 Water

STAGE(5)

RCT H 101-83-7
 SOL 141-78-6 AcOEt
 CON SUBSTAGE(1) 0.5 hours, 25 - 35 deg C
 SUBSTAGE(2) 0.5 hours, 25 - 35 deg C

PRO I 577953-88-9

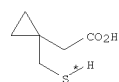
RX(5) OF 6 COMPOSED OF RX(2), RX(3)
 RX(5) G + C + H ==> P

L3 ANSWER 13 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)
 dilithium dianion of 1-(mercaptomethyl)cyclopropane acetic acid by reacting with alkyl lithium, (b) coupling the said dianion with wet mesylate to get montelukast acid in crude form, (c) obtaining DCHA salt in crude form by adding dicyclohexylamine (DCHA) to crude acid obtained in the above step (b), (d) purifying and converting the said DCHA salt in crude form to montelukast acid in pure form, and (e) reacting the pure montelukast acid in a polar protic solvent with a source of sodium ion followed by evapp. the solvent and triturating of the residue with non-polar water immiscible solvent. For instance, I•Na was obtained from the prepd. and purified I and sodium hydroxide with a yield of 98.7% (HPLC purity was 99.42%). The invention proposes industrially feasible and cost-effective process for high-yield and high-purity prepn. of I•Na.

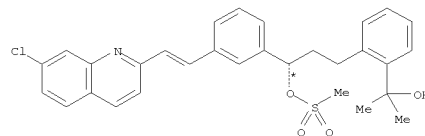
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

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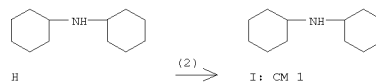
RX(2) OF 6 ...G + C + H ==> I...



G



C

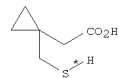


H

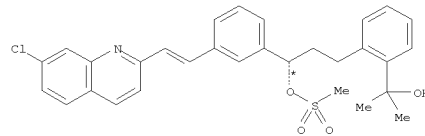
(2)

I: CM 1

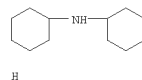
L3 ANSWER 13 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



G

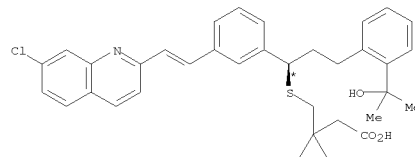


C



H

2 STEPS



P

YIELD 61%

RX(2) RCT G 162515-68-6

STAGE(1)

RGT J 109-72-8 BuLi
 SOL 109-99-9 THF, 110-54-3 Hexane
 CON SUBSTAGE(1) -15 - -10 deg C

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L3 ANSWER 13 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

STAGE(2)
 RCT C 807638-71-7
 SOL 109-99-9 THF
 CON SUBSTAGE(1) room temperature -> -5 deg C
 SUBSTAGE(2) -10 - -5 deg C
 SUBSTAGE(3) 0.25 hours, -10 - -5 deg C

STAGE(3)
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 0.5 hours, -7 - -3 deg C
 SUBSTAGE(2) 12 hours

STAGE(4)
 RGT K 7647-14-5 NaCl
 SOL 7732-18-5 Water

STAGE(5)
 RCT H 101-83-7
 SOL 141-78-6 AcOEt
 CON SUBSTAGE(1) 0.5 hours, 25 - 35 deg C
 SUBSTAGE(2) 0.5 hours, 25 - 35 deg C

PRO I 577953-88-9

RX(3)
 RCT I 577953-88-9
 RGT Q 64-19-7 AcOH
 PRO P 158966-92-8
 SOL 7732-18-5 Water, 108-88-3 PhMe
 CON SUBSTAGE(1) 30 minutes, 25 - 35 deg C
 SUBSTAGE(2) 15 minutes, 25 - 35 deg C

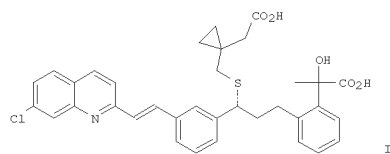
L3 ANSWER 14 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 129:254989 CASREACT
 TITLE: Quinoline diacid derivatives, and preparation
 thereof,

INVENTOR(S): for leukotriene antagonists
 Arison, Byron H.; Balani, Suresh K.; Baillie, Thomas
 A.; Dufresne, Claude
 PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Merck Frosst Canada Inc.
 SOURCE: PCT Int. Appl., 42 pp.
 CODEN: FIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9839970	A1	19980917	WO 1998-US4609	19980310
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2283101	A1	19980917	CA 1998-2283101	19980310
CA 2283101	C	20080122		
AU 9867589	A	19980929	AU 1998-67589	19980310
AU 726210	B2	20001102		
US 5952347	A	19990914	US 1998-37949	19980310
EP 971587	A1	20000119	EP 1998-912911	19980310
EP 971587	B1	20060208		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, LT, FI				
EE 9900406	A	20000417	EE 1999-406	19980310
EE 3732	B1	20020617		
JP 2001514660	T	20010911	JP 1998-539688	19980310
AT 317224	T	20060215	AT 1998-912911	19980310
ES 2256933	T3	20060716	ES 1998-912911	19980310
PRIORITY APPLN. INFO.:			US 1997-40413P	19970313
			GB 1997-11030	19970529
			WO 1998-US4609	19980310
OTHER SOURCE(S):		MARPAT 129:254989		
GI				

L3 ANSWER 14 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

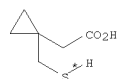


AB Compds. I are antagonists of the actions of leukotrienes. These compds. are useful as anti-asthmatic, anti-allergic, anti-inflammatory, and cytoprotective agents. They are also useful in treating angina, cerebral spasm, glomerular nephritis, hepatitis, endotoxemia, uveitis, and allograft rejection. I are biliary metabolites of montelukast sodium. Compound isolation and preparation are described.

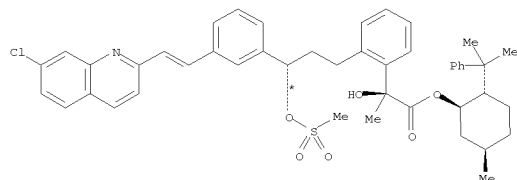
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

RX(2) OF 48 ...2 K + D + E ==> L + M...

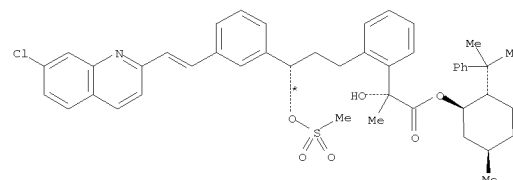


2 K



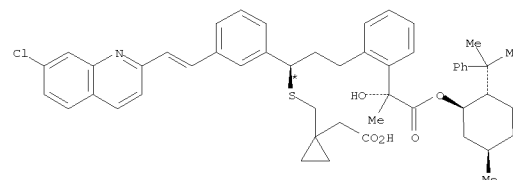
D

L3 ANSWER 14 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



E

(2) →

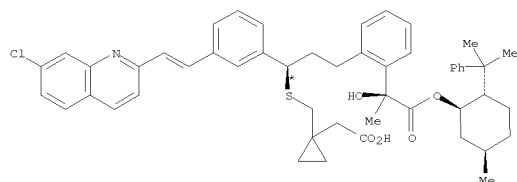


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L3 ANSWER 14 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



M

RX(2) RCT K 162515-68-6

STAGE(1)

RGT N 109-72-8 BuLi
SOL 109-99-9 THF

STAGE(2)

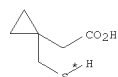
RCT D 213380-30-4, E 213380-31-5
SOL 109-99-9 THF

STAGE(3)

RGT O 12125-02-9 NH4Cl
SOL 7732-18-5 Water

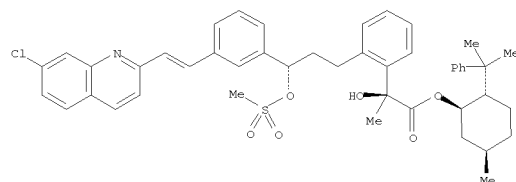
PRO L 213380-32-6, M 213380-33-7

RX(13) OF 48 COMPOSED OF RX(2), RX(3)
RX(13) 2 K + D + E ==> 2 Q

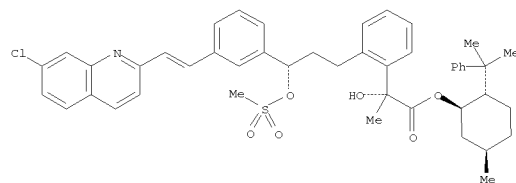


2 K

L3 ANSWER 14 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



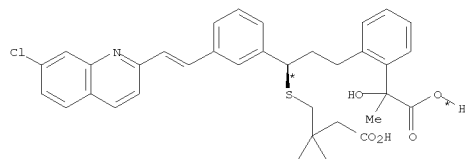
D



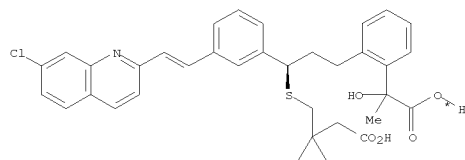
E

2
STEPS
→

L3 ANSWER 14 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



Q



Q

RX(2) RCT K 162515-68-6

STAGE(1)

RGT N 109-72-8 BuLi
SOL 109-99-9 THF

STAGE(2)

RCT D 213380-30-4, E 213380-31-5
SOL 109-99-9 THF

STAGE(3)

RGT O 12125-02-9 NH4Cl
SOL 7732-18-5 Water

PRO L 213380-32-6, M 213380-33-7

RX(3) RCT L 213380-32-6, M 213380-33-7

STAGE(1)

RGT R 1310-65-2 LiOH
SOL 64-17-5 EtOH, 7732-18-5 Water

STAGE(2)

RGT O 12125-02-9 NH4Cl, S 64-19-7 AcOH
SOL 7732-18-5 Water

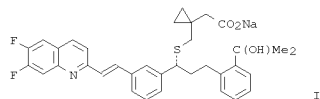
L3 ANSWER 14 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

PRO Q 213380-27-9

02/18/2009

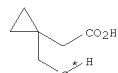
10-576,971.trn

L3 ANSWER 15 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 126:225199 CASREACT
TITLE: The enantioselective synthesis of LTD4 antagonist
L-708,738
AUTHOR(S): Sidler, Daniel R.; Sager, Jess W.; Bergan, James J.;
Wells, Kenneth M.; Bhupathy, M.; Volante, R. P.
CORPORATE SOURCE: Process Research Department, Merck Research
Laboratories, Rahway, NJ, 07065, USA
SOURCE: Tetrahedron: Asymmetry (1997), 8(1), 161-168
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB An efficient, 9-step synthesis of LTD4 antagonist L-708,738 sodium salt
(I) was described. The asym. center was set via a chiral borane
reduction
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

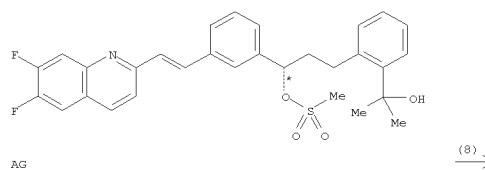
RX(8) OF 36 ...AI + AG ==> AJ



AI

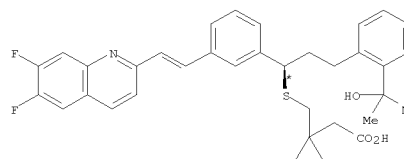
L3 ANSWER 15 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)
NTE intermediate DCHA salt prepd. and characterized

L3 ANSWER 15 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



AG

(8) →



● Na

AJ

RX(8) RCT AI 162515-68-6

STAGE(1)
RGT AK 109-72-8 BuLi
SOL 109-99-9 THF, 110-54-3 Hexane
STAGE(2)
RCT AG 188351-74-8
STAGE(3)
RGT P 64-19-7 AcOH
SOL 7732-18-5 Water, 108-88-3 PhMe
STAGE(4)
RGT AL 1310-73-2 NaOH
PRO AJ 152922-64-0

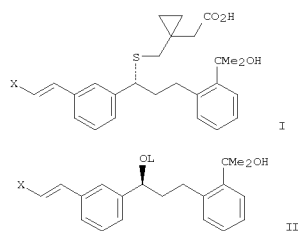
L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 123:313787 CASREACT
TITLE: Preparation of quinoline derivative leukotriene
antagonists.
INVENTOR(S): Bhupathy, Mahadevan; McNamara, James M.; Sidler,
Daniel R.; Volante, Ralph P.; Bergan, James J.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9518107	A1	19950706	WO 1994-US14858	19941222
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
TW 416948	B	20010101	TW 1994-83111982	19941221
TW 448160	B	20010801	TW 2000-89114101	19941221
CA 2179407	A1	19950706	CA 1994-2179407	19941222
AU 9514448	A	19950717	AU 1995-14448	19941222
AU 686303	B2	19980205		
EP 737186	A1	19961016	EP 1995-906106	19941222
EP 737186	B1	19980819		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CN 1139429	A	19970101	CN 1994-194671	19941222
CN 1046712	C	19991124		
JP 09507235	T	19970722	JP 1995-518152	19941222
JP 3640962	B2	20050420		
HU 76279	A2	19970728	HU 1996-1775	19941222
HU 226394	B1	20081128		
BR 9408452	A	19970805	BR 1994-8452	19941222
AT 169906	T	19980915	AT 1995-906106	19941222
ES 2122534	T3	19981216	ES 1995-906106	19941222
CN 1219535	A	19990616	CN 1998-118381	19941222
CN 1326837	C	20070718		
RU 2140909	C1	19991110	RU 1996-113796	19941222
CZ 286079	B6	20000112	CZ 1996-1878	19941222
PL 178671	B1	20000531	PL 1994-315155	19941222
RO 119018	B1	20040227	RO 1996-1312	19941222
RU 2225398	C2	20040310	RU 1999-110880	19941222
CN 101081834	A	20071205	CN 2006-10094487	19941222
US 5614632	A	19970325	US 1995-439733	19950512
FI 9602641	A	19960626	FI 1996-2641	19960626
FI 113045	B1	20040227		
HK 1009269	A1	20010824	HK 1998-109868	19980812
US 6320052	B1	20011120	US 1999-274062	19990322
LV 12313	B	19991120	LV 1999-73	19990427
PRIORITY APPLN. INFO.:			US 1993-174931	19931228
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			CN 1998-118381	19941222
			RU 1996-113796	19941222
			WO 1994-US14858	19941222

02/18/2009

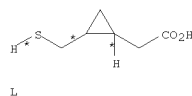
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L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)
 US 1997-943868 19971008
 OTHER SOURCE(S): MARPAT 123:313787
 GI

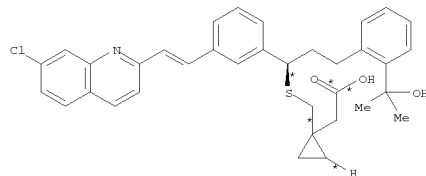
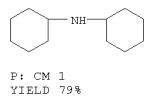
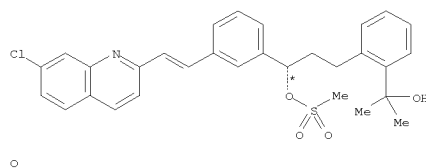
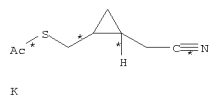


AB Title compds. (I; X = 7-chloroquinolin-2-yl, 6,7-difluoroquinolin-2-yl)
 or Na salts thereof, were prepared by generating and reacting the dilithium
 dianion of 1-mercaptomethyl-1-carboxymethylcyclopropane with (II; L =
 arylsulfonyl, alkylsulfonyl). Thus, 1-mercaptomethyl-1-carboxymethylcyclopropane (preparation given) in THF
 was treated with BuLi at < -5° and then with
 2-[2-[3(S)-[3-[2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-
 methanesulfonyloxypropyl]phenyl]-2-propanol (preparation given) and the
 mixture was aged 8.5 h at -5° to give 79% I (X = 7-chloroquinolin-2-yl),
 isolated as the dicyclohexylamine salt.
 REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

RX(4) OF 28 ...L + O ==> P

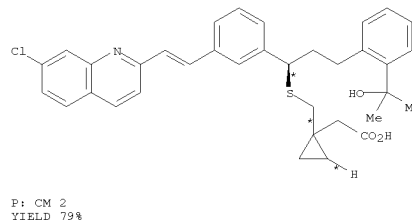
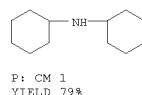
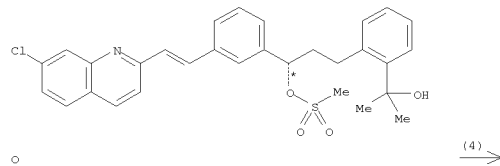


L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



RX(3) RCT K 169954-91-0
 RGT M 1310-73-2 NaOH
 PRO L 169954-92-1
 SOL 108-88-3 PhMe, 7732-18-5 Water

L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



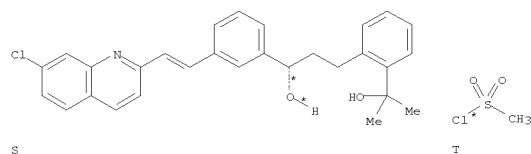
RX(4) RCT L 169954-92-1, O 169954-93-2
 RGT Q 109-72-8 BuLi
 PRO P 169954-94-3
 SOL 109-99-9 THF
 NTE -5°, 8.5 h

RX(10) OF 28 COMPOSED OF RX(3), RX(4)
 RX(10) K + O ==> P

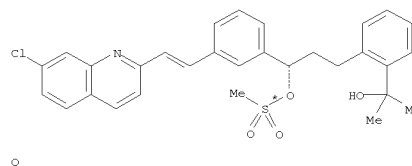
L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

RX(4) RCT L 169954-92-1, O 169954-93-2
 RGT Q 109-72-8 BuLi
 PRO P 169954-94-3
 SOL 109-99-9 THF
 NTE -5°, 8.5 h

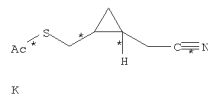
RX(17) OF 28 COMPOSED OF REACTION SEQUENCE RX(5), RX(4)
 AND REACTION SEQUENCE RX(3), RX(4)
 ...S + T ==> O...
 ...K + O ==> P



2
STEPS



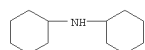
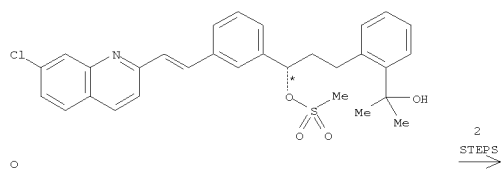
START NEXT REACTION SEQUENCE



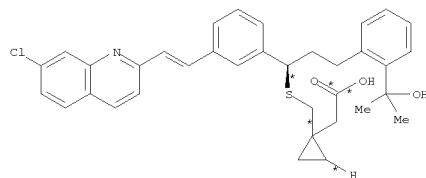
02/18/2009

10-576,971.trn

L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



P: CM 1
YIELD 79%



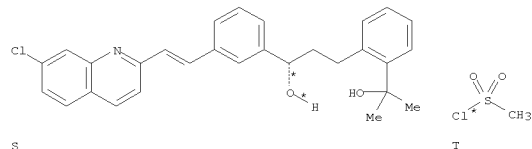
P: CM 2
YIELD 79%

RX(5) RCT S 142569-70-8, T 124-63-0
RGT D 7087-68-5 EtN(Pr-1)2
PRO O 169954-93-2
SOL 108-88-3 PhMe, 75-05-8 MeCN
RX(3) RCT K 169954-91-0
RGT M 1310-73-2 NaOH
PRO L 169954-92-1
SOL 108-88-3 PhMe, 7732-18-5 Water
RX(4) RCT L 169954-92-1, O 169954-93-2

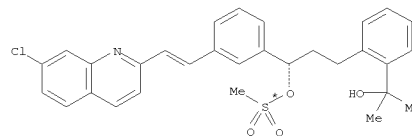
L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

RGT Q 109-72-8 BuLi
PRO P 169954-94-3
SOL 109-99-9 THF
NTE -5°, 8.5 h

RX(18) OF 28 COMPOSED OF REACTION SEQUENCE RX(5), RX(4)
AND REACTION SEQUENCE RX(6), RX(3), RX(4)
...S + T ==> O...
...G + V + O ==> P

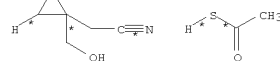


3
STEPS



O

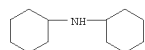
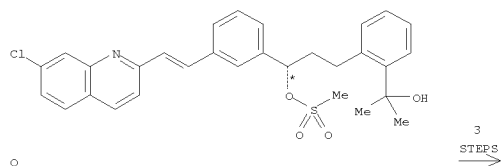
START NEXT REACTION SEQUENCE



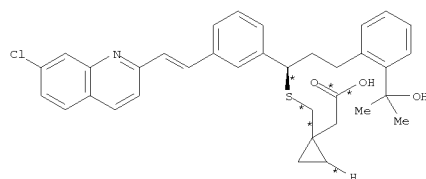
G

V

L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



P: CM 1
YIELD 79%



P: CM 2
YIELD 79%

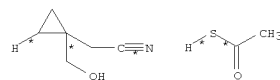
RX(5) RCT S 142569-70-8, T 124-63-0
RGT D 7087-68-5 EtN(Pr-1)2
PRO O 169954-93-2
SOL 108-88-3 PhMe, 75-05-8 MeCN
RX(6) RCT G 152922-71-9
STAGE(1)
RGT W 121-44-8 Et3N, T 124-63-0 MeSO2Cl
SOL 68-12-2 DMF, 108-88-3 PhMe
STAGE(2)
RCT V 507-09-5

L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

PRO K 169954-91-0

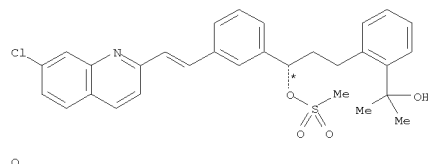
RX(3) RCT K 169954-91-0
RGT M 1310-73-2 NaOH
PRO L 169954-92-1
SOL 108-88-3 PhMe, 7732-18-5 Water
RX(4) RCT L 169954-92-1, O 169954-93-2
RGT Q 109-72-8 BuLi
PRO P 169954-94-3
SOL 109-99-9 THF
NTE -5°, 8.5 h

RX(20) OF 28 COMPOSED OF RX(6), RX(3), RX(4)
RX(20) G + V + O ==> P

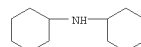


G

V



O

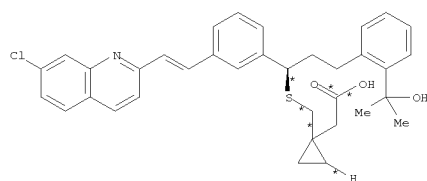


P: CM 1
YIELD 79%

02/18/2009

10-576,971.trn

L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



P: CM 2
YIELD 79%

RX(6) RCT G 152922-71-9

STAGE(1)

RGT W 121-44-8 Et3N, T 124-63-0 MeSO2Cl
SOL 68-12-2 DMF, 108-88-3 PhMe

STAGE(2)

RCT V 507-09-5

PRO K 169954-91-0

RX(3) RCT K 169954-91-0

RGT M 1310-73-2 NaOH

PRO L 169954-92-1

SOL 108-88-3 PhMe, 7732-18-5 Water

RX(4) RCT L 169954-92-1, O 169954-93-2

RGT Q 109-72-8 BuLi

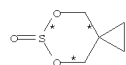
PRO P 169954-94-3

SOL 109-99-9 THF

NTE -5°, 8.5 h

RX(21) OF 28 COMPOSED OF RX(2), RX(6), RX(3), RX(4)

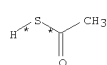
RX(21) B + F + V + O ==> P



B



F



V

L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

SOL 68-12-2 DMF, 108-88-3 PhMe

STAGE(2)

RCT V 507-09-5

PRO K 169954-91-0

RX(3) RCT K 169954-91-0

RGT M 1310-73-2 NaOH

PRO L 169954-92-1

SOL 108-88-3 PhMe, 7732-18-5 Water

RX(4) RCT L 169954-92-1, O 169954-93-2

RGT Q 109-72-8 BuLi

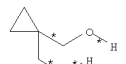
PRO P 169954-94-3

SOL 109-99-9 THF

NTE -5°, 8.5 h

RX(23) OF 28 COMPOSED OF RX(1), RX(2), RX(6), RX(3), RX(4)

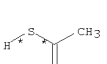
RX(23) A + F + V + O ==> P



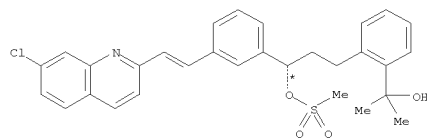
A



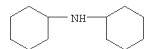
F



V

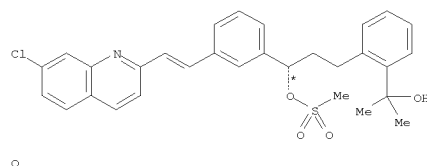


O

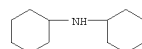
5
STEPS

P: CM 1
YIELD 79%

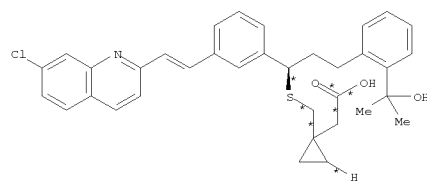
L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



O

4
STEPS

P: CM 1
YIELD 79%



P: CM 2
YIELD 79%

RX(2) RCT B 89729-09-9, F 143-33-9

RGT H 7681-82-5 NaI

PRO G 152922-71-9

SOL 108-88-3 PhMe, 68-12-2 DMF

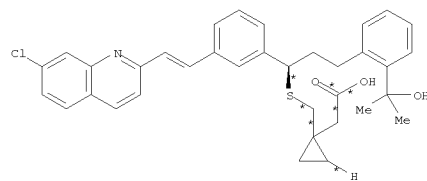
NTE 70°

RX(6) RCT G 152922-71-9

STAGE(1)

RGT W 121-44-8 Et3N, T 124-63-0 MeSO2Cl

L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



P: CM 2
YIELD 79%

RX(1) RCT A 39590-81-3

RGT C 7719-09-7 SOCl2, D 7087-68-5 EtN(Pr-i)2

PRO B 89729-09-9

SOL 75-09-2 CH2Cl2

NTE 0-5°

RX(2) RCT B 89729-09-9, F 143-33-9

RGT H 7681-82-5 NaI

PRO G 152922-71-9

SOL 108-88-3 PhMe, 68-12-2 DMF

NTE 70°

RX(6) RCT G 152922-71-9

STAGE(1)

RGT W 121-44-8 Et3N, T 124-63-0 MeSO2Cl

SOL 68-12-2 DMF, 108-88-3 PhMe

STAGE(2)

RCT V 507-09-5

PRO K 169954-91-0

RX(3) RCT K 169954-91-0

RGT M 1310-73-2 NaOH

PRO L 169954-92-1

SOL 108-88-3 PhMe, 7732-18-5 Water

RX(4) RCT L 169954-92-1, O 169954-93-2

RGT Q 109-72-8 BuLi

PRO P 169954-94-3

SOL 109-99-9 THF

NTE -5°, 8.5 h

RX(24) OF 28 COMPOSED OF REACTION SEQUENCE RX(5), RX(4)

AND REACTION SEQUENCE RX(2), RX(6), RX(3), RX(4)

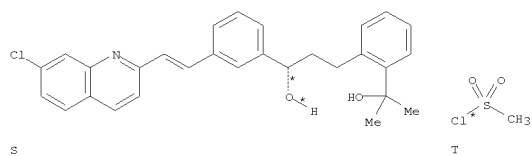
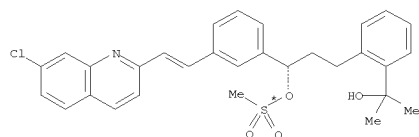
...S + T ==> O...

...B + F + V + O ==> P

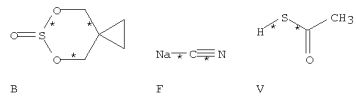
02/18/2009

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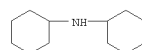
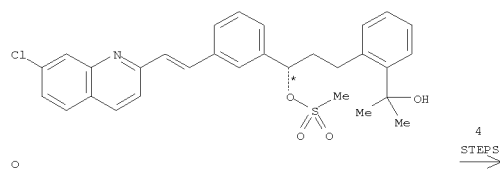
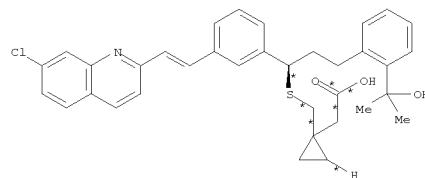
L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

4
STEPS

START NEXT REACTION SEQUENCE



L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

P: CM 1
YIELD 79%P: CM 2
YIELD 79%

RX(5) RCT S 142569-70-8, T 124-63-0
RGT D 7087-68-5 EtN(Pr-1)2
PRO O 169954-93-2
SOL 108-88-3 PhMe, 75-05-8 MeCN

RX(2) RCT B 89729-09-9, F 143-33-9
RGT H 7681-82-5 NaI
PRO G 152922-71-9
SOL 108-88-3 PhMe, 68-12-2 DMF
NTE 70°

L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

RX(6) RCT G 152922-71-9

STAGE(1)
RGT W 121-44-8 Et3N, T 124-63-0 MeSO2Cl
SOL 68-12-2 DMF, 108-88-3 PhMe

STAGE(2)
RCT V 507-09-5

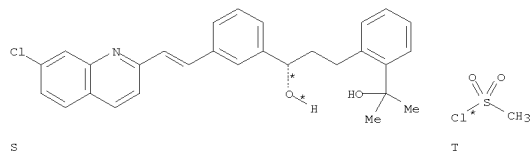
PRO K 169954-91-0

RX(3) RCT K 169954-91-0
RGT M 1310-73-2 NaOH
PRO L 169954-92-1
SOL 108-88-3 PhMe, 7732-18-5 Water

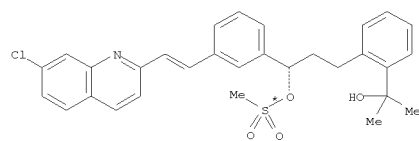
RX(4) RCT L 169954-92-1, O 169954-93-2
RGT Q 109-72-8 BuLi
PRO P 169954-94-3
SOL 109-99-9 THF
NTE -5°, 8.5 h

RX(25) OF 28 COMPOSED OF REACTION SEQUENCE RX(5), RX(4)
AND REACTION SEQUENCE RX(1), RX(2), RX(6), RX(3), RX(4)

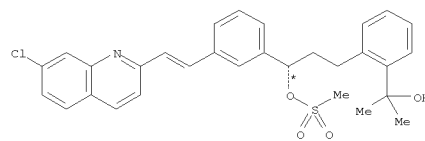
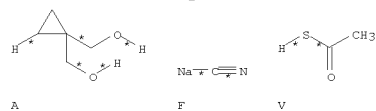
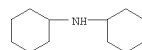
...S + T ==> O...
...A + F + V + O ==> P

5
STEPS

L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



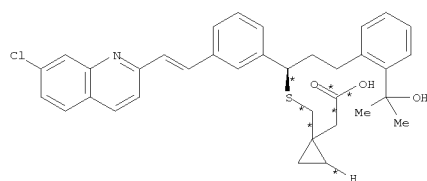
START NEXT REACTION SEQUENCE

5
STEPSP: CM 1
YIELD 79%

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L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



P: CM 2
YIELD 79%

RX(5) RCT S 142569-70-8, T 124-63-0
RGT D 7087-68-5 EtN(Pr-i)2
PRO O 169954-93-2
SOL 108-88-3 PhMe, 75-05-8 MeCN

RX(1) RCT A 39590-81-3
RGT C 7719-09-7 SOCl2, D 7087-68-5 EtN(Pr-i)2
PRO B 89729-09-9
SOL 75-09-2 CH2Cl2
NTE 0-5°

RX(2) RCT B 89729-09-9, F 143-33-9
RGT H 7681-82-5 NaI
PRO G 152922-71-9
SOL 108-88-3 PhMe, 68-12-2 DMF
NTE 70°

RX(6) RCT G 152922-71-9

STAGE(1)
RGT W 121-44-8 Et3N, T 124-63-0 MeSO2Cl
SOL 68-12-2 DMF, 108-88-3 PhMe

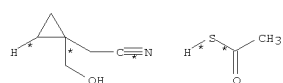
STAGE(2)
RCT V 507-09-5

PRO K 169954-91-0

RX(3) RCT K 169954-91-0
RGT M 1310-73-2 NaOH
PRO L 169954-92-1
SOL 108-88-3 PhMe, 7732-18-5 Water

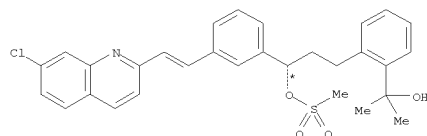
RX(4) RCT L 169954-92-1, O 169954-93-2
RGT Q 109-72-8 BuLi

L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



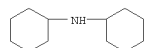
G

V

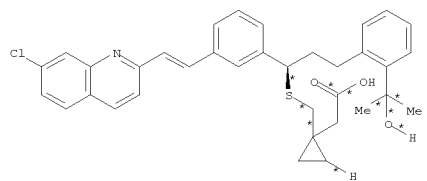


O

3
STEPS



P: CM 1
YIELD 79%



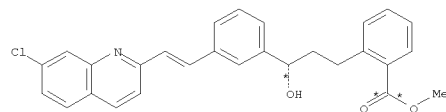
P: CM 2
YIELD 79%

RX(7) RCT X 142569-69-5, Y 75-16-1
RGT Z 7790-86-5 CeCl3
PRO S 142569-70-8
SOL 109-99-9 THF, 108-88-3 PhMe

L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

PRO P 169954-94-3
SOL 109-99-9 THF
NTE -5°, 8.5 h

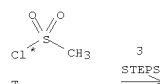
RX(26) OF 28 COMPOSED OF REACTION SEQUENCE RX(7), RX(5), RX(4)
AND REACTION SEQUENCE RX(6), RX(3), RX(4)
...X + 2 Y + T ==> O...
...G + V + O ==> P



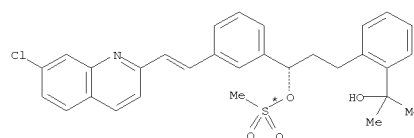
X



2 Y



T



O

START NEXT REACTION SEQUENCE

L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

RX(5) RCT S 142569-70-8, T 124-63-0
RGT D 7087-68-5 EtN(Pr-i)2
PRO O 169954-93-2
SOL 108-88-3 PhMe, 75-05-8 MeCN

RX(6) RCT G 152922-71-9

STAGE(1)
RGT W 121-44-8 Et3N, T 124-63-0 MeSO2Cl
SOL 68-12-2 DMF, 108-88-3 PhMe

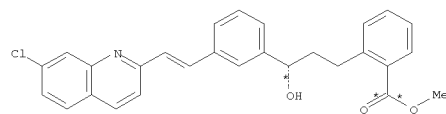
STAGE(2)
RCT V 507-09-5

PRO K 169954-91-0

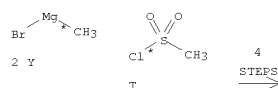
RX(3) RCT K 169954-91-0
RGT M 1310-73-2 NaOH
PRO L 169954-92-1
SOL 108-88-3 PhMe, 7732-18-5 Water

RX(4) RCT L 169954-92-1, O 169954-93-2
RGT Q 109-72-8 BuLi
PRO P 169954-94-3
SOL 109-99-9 THF
NTE -5°, 8.5 h

RX(27) OF 28 COMPOSED OF REACTION SEQUENCE RX(7), RX(5), RX(4)
AND REACTION SEQUENCE RX(2), RX(6), RX(3), RX(4)
...X + 2 Y + T ==> O...
...B + F + V + O ==> P



X



2 Y

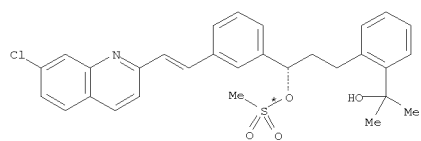
T

4
STEPS

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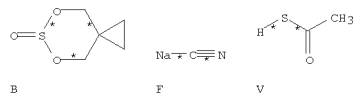
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L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



O

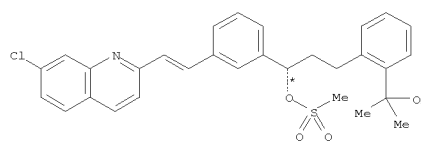
START NEXT REACTION SEQUENCE



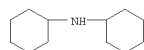
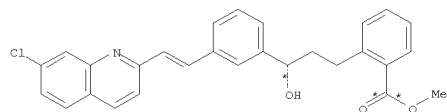
B

F

V



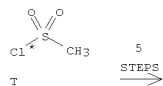
O

4
STEPSP: CM 1
YIELD 79%L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)
SOL 109-99-9 THF
NTE -5°, 8.5 hRX(28) OF 28 COMPOSED OF REACTION SEQUENCE RX(7), RX(5), RX(4)
AND REACTION SEQUENCE RX(1), RX(2), RX(6), RX(3), RX(4)
...X + 2 Y + T ==> O...
...A + F + V + O ==> P

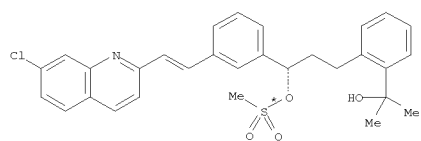
X



2 Y



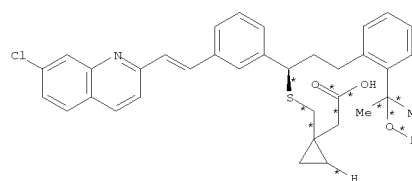
T

5
STEPS

O

START NEXT REACTION SEQUENCE

L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

P: CM 2
YIELD 79%RX(7) RCT X 142569-69-5, Y 75-16-1
RGT Z 7790-86-5 CeCl3
PRO S 142569-70-8
SOL 109-99-9 THF, 108-88-3 PhMeRX(5) RCT S 142569-70-8, T 124-63-0
RGT D 7087-68-5 EtN(Pr-1)2
PRO O 169954-93-2
SOL 108-88-3 PhMe, 75-05-8 MeCNRX(2) RCT B 89729-09-9, F 143-33-9
RGT H 7681-82-5 NaI
PRO G 152922-71-9
SOL 108-88-3 PhMe, 68-12-2 DMF
NTE 70°

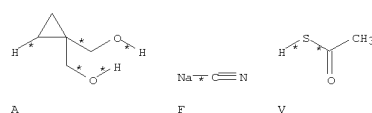
RX(6) RCT G 152922-71-9

STAGE(1)
RGT W 121-44-8 Et3N, T 124-63-0 MeSO2C1
SOL 68-12-2 DMF, 108-88-3 PhMeSTAGE(2)
RCT V 507-09-5

PRO K 169954-91-0

RX(3) RCT K 169954-91-0
RGT M 1310-73-2 NaOH
PRO L 169954-92-1
SOL 108-88-3 PhMe, 7732-18-5 WaterRX(4) RCT L 169954-92-1, O 169954-93-2
RGT Q 109-72-8 BuLi
PRO F 169954-94-3

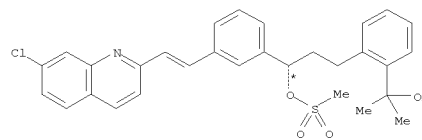
L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)



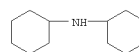
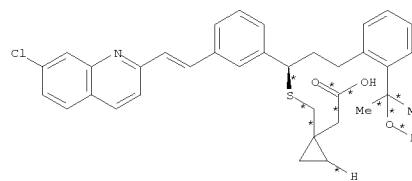
A

F

V



O

5
STEPSP: CM 1
YIELD 79%P: CM 2
YIELD 79%RX(7) RCT X 142569-69-5, Y 75-16-1
RGT Z 7790-86-5 CeCl3
PRO S 142569-70-8
SOL 109-99-9 THF, 108-88-3 PhMe

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L3 ANSWER 16 OF 16 CASREACT COPYRIGHT 2009 ACS on STN (Continued)

RX(5) RCT S 142569-70-8, T 124-63-0
RGT D 7087-68-5 EtN(Pr-i)2
PRO O 169954-93-2
SOL 108-88-3 PhMe, 75-05-8 MeCN

RX(1) RCT A 39590-81-3
RGT C 7719-09-7 SOCl2, D 7087-68-5 EtN(Pr-i)2
PRO B 89729-09-9
SOL 75-09-2 CH2Cl2
NTE 0-5°

RX(2) RCT B 89729-09-9, F 143-33-9
RGT H 7681-82-5 NaI
PRO G 152922-71-9
SOL 108-88-3 PhMe, 68-12-2 DMF
NTE 70°

RX(6) RCT G 152922-71-9
STAGE(1)
RGT W 121-44-8 Et3N, T 124-63-0 MeSO2Cl
SOL 68-12-2 DMF, 108-88-3 PhMe

STAGE(2)
RCT V 507-09-5

PRO K 169954-91-0

RX(3) RCT K 169954-91-0
RGT M 1310-73-2 NaOH
PRO L 169954-92-1
SOL 108-88-3 PhMe, 7732-18-5 Water

RX(4) RCT L 169954-92-1, O 169954-93-2
RGT Q 109-72-8 BuLi
PRO P 169954-94-3
SOL 109-99-9 THF
NTE -5°, 8.5 h

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